NAVAL MEDICAL RESEARCH UNIT– DAYTON

Subacute Effects of Inhaled Jet Fuel-A (JET A) on Airway and Immune Function in Rats

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The experiments reported herein were conducted in compliance with the Animal Welfare Act and in accordance with the principles set forth in the "Guide for the Care and Use of Laboratory Animals," Institute of Laboratory Animals Resources, National Research Council, National Academy Press, 1996.

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SUMMARY

Two studies were conducted to assess the potential airway and immune effects following subacute (14-day) exposure of female rats to 500, 1000 or 2000 mg/m^3 of Jet-A for 4 hrs/day. The first study used Sprague-Dawley rats; the second study included both Fischer 344 (F344) and Sprague-Dawley rats.

In the first study, exposure to 2000 mg/m^3 jet fuel may have caused significant upper airway inflammation on day 7 post-exposure, as indicated by elevated protein and lactate dehydrogenase in nasal lavage fluid, but any inflammation resolved by day 14 post-exposure. No significant impact on immune cell populations in the spleens was observed. The only organ weight effect that was consistently identified was a decrease in heart weight at 2000 mg/m^3. The histological examination showed no evidence of infectious or toxic effect, and the occasional presence inflammation or mineralization was clinically insignificant.

In the second study, body weights of the F344 rats in the 2000 mg/m^3 group were depressed, as compared to the controls, at the end of the exposure. Some lung lavage fluid markers were increased at 24 hrs after the final exposure, indicating possible airway injury/inflammation. However, no test article histological changes were observed in the lungs, nasal cavities, or any other tissue of any of the jet fuel exposed animals.

Overall, these studies demonstrated limited evidence of effects of 14 days of exposure to Jet A on the airways, immune system, or any other organ or system of female Sprague-Dawley and F344 rats, with no remarkable differences between strains.

KEY WORDS AND PHRASES

Jet fuel, Jet A, rats, immunotoxicity, lung injury, bronchoalveolar lavage, nasal lavage, inhalation, two-week, vapor and aerosol

INTRODUCTION

Background/Military Relevance

Each year over 2 million military and civilian personnel are occupationally exposed to jet propulsion fuel-8 (JP-8), JP-8+10, JP-5, or to the civil aviation equivalents Jet Fuel-A (Jet A) or Jet A-1 (Ritchie *et al.*, 2003). Jet fuels are among the most common sources of military and nonmilitary occupational chemical exposures. Jet fuel is a kerosene based hydrocarbon fuel which contains complex mixtures of up to 260 aliphatic and aromatic hydrocarbon compounds, including varying concentrations of potential toxicants such as benzene, n-hexane, toluene, xylenes, trimethylpentane, methoxyethanol, and naphthalenes (Ritchie *et al.*, 2003). Jet A serves as the base fuel for blending JP-8 military fuels.

Military and civilian personnel can be occupationally exposed to the raw fuel, vapor phase, aerosol phase, or fuel combustion exhaust through dermal absorption, inhalation, or oral ingestion. A number of published studies have reported short-term or persisting health effects from acute, subchronic or chronic jet fuel exposure in humans and/or animals. Effects of jet fuel have been reviewed by Ritchie *et al.* (2003). Jet fuel has been linked to small numbers of cardiac events and neurobehavioral effects (disorientation) in humans (Knave *et al.*, 1976) and liver effects in male rats (changes in aspartate aminotransferase, AST) (Mattie *et al.*, 1995). In 1996, the Committee on Toxicology of the National Research Council reviewed the toxicity of military fuels, including jet fuels, and identified a need for additional toxicology studies (NRC, 1996). The work reported here focuses on the toxicity of Jet A to the respiratory and immune systems.

Physiological, biochemical, cellular, and morphological lung injury have been observed in mice exposed to aerosolized JP-8 by inhalation (Robledo *et al.*, 2000). Interpretation of existing inhalation studies is complicated by uncertainties regarding the test atmospheres. The vapor produced for inhalation exposures contains a portion, but not necessarily all, of the chemical constituents of the parent liquid. If the fuel is sprayed into the air, the droplets of spray also partially evaporate. The remaining droplets and the vaporized fuel do not have the same chemical composition, with the aerosol phase enriched in low vapor pressure components and the vapor phase enriched in the high vapor pressure components. In many of the inhalation studies, either only the vapor portion or only the aerosol portion of the atmosphere was measured (Tremblay *et al.*, 2010). As a result, many inhalation exposures that were considered "low" to "moderate" were actually much higher than reported.

Inhalation jet fuel studies suggest that jet fuel may also be immunotoxic. As defined by U.S. EPA (1996), "'Immuntoxicity' refers to the ability of a test substance to induce dysfunction or inappropriate suppression or stimulatory responses in components of the immune system." A study of Air Force fuel system maintenance workers found that those identified as having "high" exposure (n = 45) (exposure level assigned based on expert consensus of various job title categorization) had significantly higher counts of white blood cells, neutrophils, and monocytes

as compared to the "low" exposure group (n = 78). Elevated breathing zone and post-exposure breath levels of naphthalene (a known component of JP-8, used as a surrogate for jet fuel exposure) support the categorization of the workers into the designated categories. No differences were found with respect to total levels of lymphocytes, T-cells, T-helper cells, T-suppressor cells, natural killer cells, and B-cells (Rhodes *et al.*, 2003). Mice exposed for 1 hour to 1000 mg/m^3 (measured as aerosol particulates only) experienced significant immune organ weight loss and loss of viable immune cells by 1 hour post-exposure (Harris *et al.*, 2002).

Dermal studies have yielded conflicting results. Studies of dermal application of jet fuel in mice have been interpreted as indicating immune suppression (Ullrich, 1999; Ullrich and Lyons, 2000; Ramos *et al.*, 2009). A dermal study in female Sprague-Dawley rats, however, found jet fuel to lack immunotoxicity. Mann *et al.* (2008) suggest that the differences between studies may be due to species susceptibility differences or factors such as the minimization of irritancy in their study, thus potentially eliminating changes in immune system parameters that are secondary to inflammation. In laboratory animals, cutaneous JP-8 exposures cause irritation. Hydrocarbons, a main constituent of jet fuels, are also known to cause skin cancer with repeated dermal application (reviewed by McDougal and Rogers, 2004).

Changes in cellularity and biomarkers of airway injuries offer valuable information about hazards of inhaled compounds. Thus, lymphocyte numbers and differential, important enzymes and other biomarkers found in bronchoalveolar lavage fluids (BALf) and nasal lavage fluid were investigated for Jet A exposed animals. An increase of total protein in lavage fluid would indicate an increase in both epithelial and endothelial permeability. Should such an increase be accompanied by an influx of neutrophils, this finding would be evidence of an inflammatory response to injury (Henderson *et al.*, 1985). Extracellular cytoplasmic enzymes, such as lactate dehydrogenase (LDH), are good indicators of cytotoxicity (Henderson, 1988 and 1989). β-Glucuronidase (βgluc) is an indicator of phagocytic activity, macrophage recruitment, and lysosomal injury. An increase in the activity of these enzymes correlates well with the generalized pulmonary toxicity of inhaled particles/aerosols (Beck *et al.*, 1982; Henderson, 1988). Batteries of several assays have been proposed to evaluate the potential of chemicals to affect the immune system (e.g., U.S. EPA, 1996). Functional assays (e.g., plaque-forming cell assays, assays of natural killer cell activity, T-cell proliferation assays, and delayed hypersensitivity response) were deemed to be outside the desired scope of the investigation described herein. Immune organ weights, additional lavage fluid markers (e.g., cytokines relevant to the inflammation process), and spleen cell phenotyping were included to provide information on potential immune system effects of Jet A inhalation.

Objective

The purpose of these studies was to determine the subacute effects of inhaled Jet A on the airways and the immune system of exposed rats. The second phase of the study was designed to

determine if inbred Fischer 344 (F344) rats were more sensitive than outbred Sprague-Dawley rats to pulmonary and immune effects following exposure to jet fuel aerosol/vapor.

METHODS, ASSUMPTIONS, AND PROCEDURES

Phase 1 Toxicity Study

Test Material

Jet A is a commodity fuel produced by distillation of raw petroleum by all of the major oil companies. It is virtually identical to the military fuel JP-8 except for an additive package that can contain multiple additives (e.g., fuel system icing inhibitor, anti-corrosion, static suppression, metal chelator components). It is defined by the boiling point range of the chemicals in the fuel, but not by specific chemical composition. The particular chemicals found in a given sample of fuel depend on the source of the oil used in its manufacture. This study used fuel provided by five of the major oil companies (blend POSF-4658, Chevron, Shell Oil, Exxon Mobil, CITGO, and Marathon Ashland). By special arrangement, drums of Jet A fuel were shipped to the Air Force Research Laboratory Fuels Branch at Wright-Patterson Air Force Base who mixed them and have stored several hundred gallons of the fuel for research purposes.

Study Design and Implementation

The overall study design is depicted in **Figure 1**. The three observation time points were to detect the immediate response to the test material (0-3 days) and a slightly longer time after inhalation to determine if the immediate response persists (e.g., 4-14 days) (Driscoll *et al.*, 2000). Intact young adult female Sprague-Dawley rats (n = 128; 24/group; age 7-8 weeks; Charles River Laboratories, Wilmington, MA) were quarantined for a period of 14 days, including a 3-day period of acclimation to the exposure chambers, and randomly assigned to exposure groups. Female rats were used to fill a data gap with respect to information on toxicity of jet fuel to this gender (*e.g.*, Rossi *et al.*, 2001, and Pfaff *et al*., 1995 used male rats only). Also, female rats are preferred for immunotoxicity evaluation due to their greater immune response, compared to males (Mann *et al.*, 2008). Cannulated female Sprague-Dawley rats (an additional 8 animals/group; age 11-12 weeks, Charles River Laboratories, Wilmington, MA) had jugular vein catheters to facilitate blood sampling prior to and during the 14 day exposure. They were not part of the 14-day post-exposure observation period and are not included in **Figure 1**. The quarantine period for these animals was limited to 3 days due to infection/mortality concerns for cannulated rats. A separate group of naïve controls (n = 32) were housed separately in an Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC) International-approved animal facility for the duration of the study and were not transported to the exposure room or placed in inhalation chambers.

Exposure concentrations were selected after a consortium of scientists (American Petroleum Institute, Naval Heath Research Center/Environmental Health Effects Laboratory, ManTech/Alion, Geo-Centers and Air Force) reviewed and discussed available literature and

related issues. Concentrations of 500, 1000 or 2000 mg/m^3 were considered to be representative of Jet A inhalation exposure hazards to flight line and maintenance personnel (Hays *et al.*, 1995; Tu *et al.*, 2004).

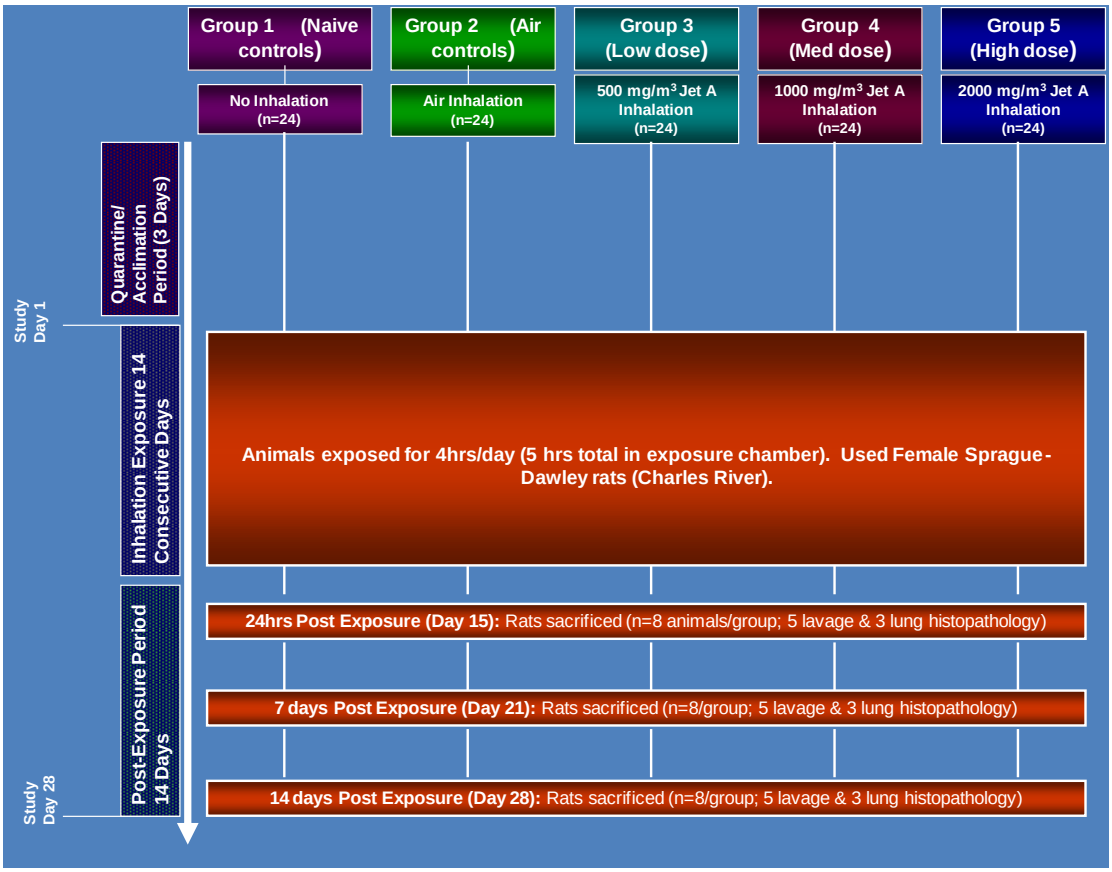

Figure 1. Study design

To generate the test atmosphere, jet fuel was pumped from a glass bottle using a FMI Model QG20 pump with a Q1CKC pump head (FMI Inc., Syosett, NY) into the fuel input port of a Sonimist® (**Figure 2**) ultrasonic spray nozzle (Misonix, Inc., Model HSS-600-1, Farmingdale, NY). An air line set to 40 pounds per square inch (psi) pressure was attached to the side arm of the Sonimist®. At this pressure, the spray nozzle developed an air flow of approximately 20 liters per minute (lpm) through the nebulizer. This air flow, coupled with the nozzle design, created an ultrasonic whistle which aerosolized the droplets of jet fuel being formed at the end of the nozzle and carried them into the generation system. A two foot length of four inch PVC pipe contained the spray pattern. The pipe was reduced in size to accept an orifice plate which measured flow rate by the pressure drop across the plate. The pipe diameter was reduced a final time to ½ inch and the aerosolized jet fuel was transported to the chamber where it was injected counter current into the main chamber flow.

During the initial 14 day study, this generator design was found to be inadequate to deliver 2000 mg/m^3 of jet fuel to the high chamber. Before the second 14 day study (described below),

several modifications were made to the generation system on the high chamber. The nebulizer was changed to a Sonimist® model HSS-600-2, which had a greater fuel throughput. However, at this higher flow volume, there was an excess jet fuel accumulation in the system piping. To help relieve constrictions to flow, the orifice plate was removed and the pipe diameter to the chamber was increased to 0.75 inches. With these modifications it was possible to attain the 2000 mg/m^3 required for this chamber while reducing jet fuel losses in the system.

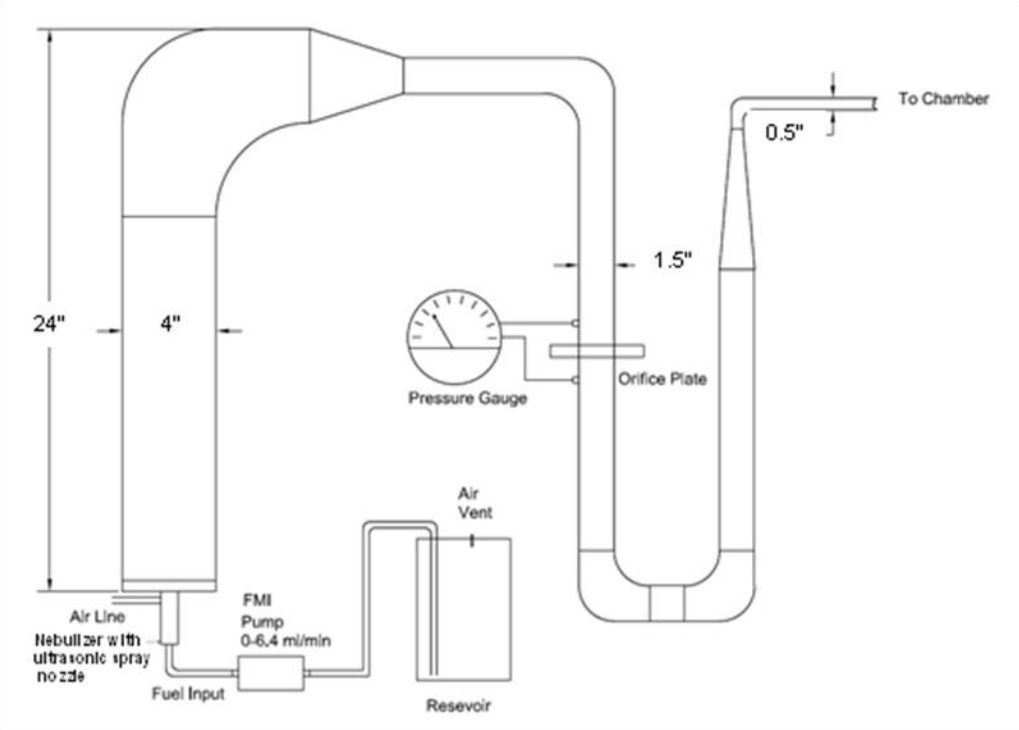

Figure 2. Schematic of jet fuel generation system used for Phase 1 toxicity testing

The exposure systems for jet fuel studies consisted of 690 liter toxic hazard research units (THRU) chambers (**Figure 3)**. These chambers were operated at one to two inches of water sub-ambient with a total flow of 180 lpm coming from the combination of the generator input and the main air flow. The main air flow was supplied by two Spencer vortex blowers (model VB-030SB-012, Windsor, CT), one providing input air and one handling exhaust flow.

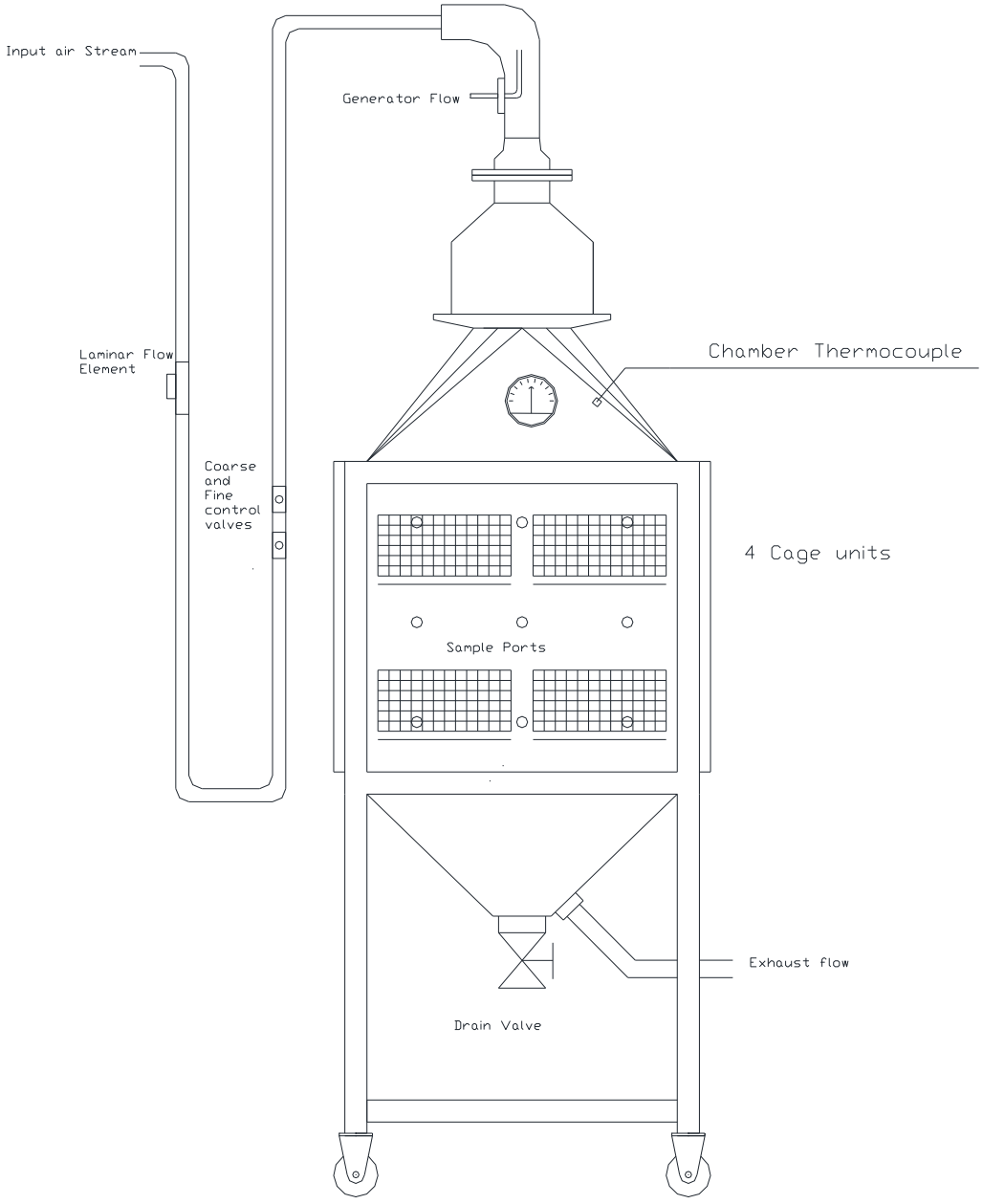

Figure 3. Schematic of THRU chamber design

The generator air flow (20 lpm, described above) was combined with 160 lpm of main air flow to achieve a total flow of 180 lpm in the chamber. The exhaust air flow was adjusted to maintain a

slightly negative- one to two inches of water- sub-ambient pressure inside of the chamber as measured with a magnehelic pressure gauge (Dwyer Instruments, Champlain, NY) attached to the upper plenum of the chamber. Airflow through the chambers was controlled with mechanical valves which were adjusted to obtain the desired flow rate. Flow rate was monitored on the input side of the chamber using a laminar flow unit (Teledyne-Hastings, model LSD58D, Hampton, VA), and the signal was monitored using a Hastings (Model 40) monitor. The chamber system schematic is depicted in **Figure 4**.

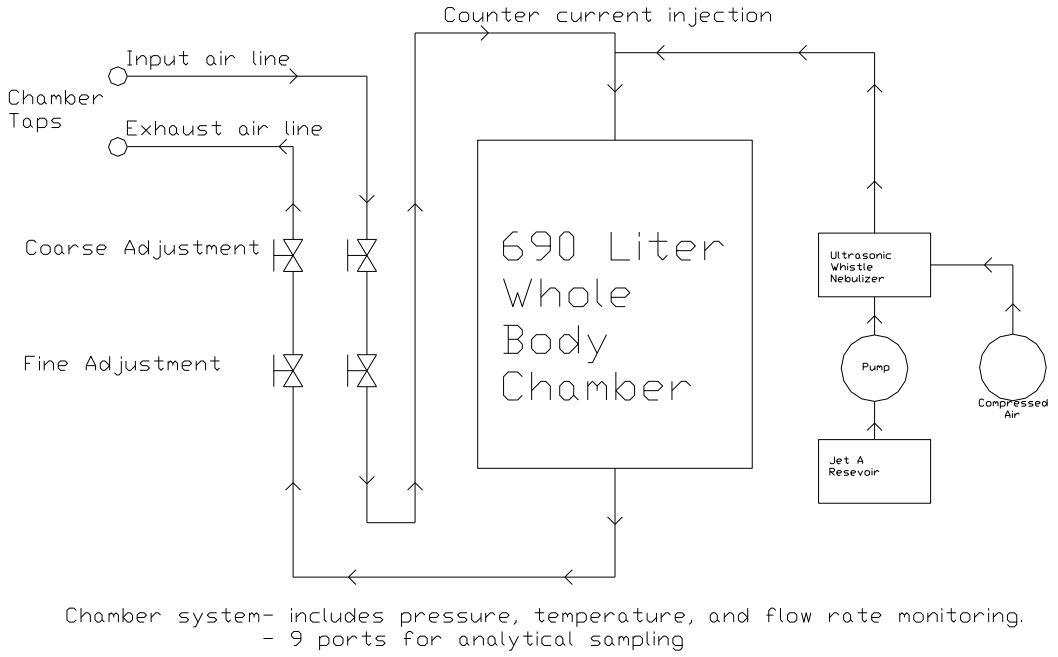

Figure 4. Schematic of exposure control system

The back of the chamber had 9 ports, which could be used for various sampling devices. Attached to one port was a calibrated (Reboulet *et al.*, 2007, 2009) Miran 1A long path infrared spectrophotometer (IR) equipped with a 0.75 to 20 meter variable path length gas cell. The path length was adjusted to give a suitable strength signal depending on the concentration being measured. Prior to entering the IR, the aerosol portion of the sample was removed using a high efficiency particulate air (HEPA) filter cartridge. The IR outputs a 0-5volt DC signal which was sent to a strip chart recorder to monitor the jet fuel concentrations in the chamber. Using a calibration curve, the voltage output was converted into the corresponding concentration values during data processing. In addition to continuous, real time IR monitoring, chamber vapor concentrations were monitored by gas liquid chromatography (GC) head space analysis (grab samples analyzed twice per run, three samples per chamber); the aerosol mass and size (mass

median aerodynamic diameter, MMAD) were determined from filter samples (47 mm glass fiber filters) and Lovelace cascade impactor analysis, respectively.

The rats were placed into the whole-body inhalation chambers and exposed to nominal concentrations of 500, 1000 or 2000 mg/m^3 Jet A vapor/aerosol or air (control) for 4 hrs/day for 14 consecutive days. Within each chamber, the cages were rotated daily to compensate for any differences in environment or exposure concentrations within the chamber.

Study Endpoints

Clinical chemistry endpoints (**Table 1**) were measured in blood drawn from indwelling jugular catheters on the day prior to exposure (PRE), at exposure day 7 (the midpoint of the study, MID), and exposure day 14 (termination of study, TS).

Table 1. Clinical Chemistry Endpoints Measured

Parameter	Definition
AST	Aspartate aminotransferase
ALT	Alanine aminotransferase
ALP	Alkaline phosphatase
PHOS	Phosphorus
LDH	Lactate dehydrogenase
TBIL	Total bilirubin
CREA	Creatinine
BUN	Blood urea nitrogen
TP	Total protein

Twenty-four hours, 7 days, and 14 days after the last inhalation exposure (Study Days 15, 21, and 28; **Figure 1**), 40 animals (n = 8/group) were given a dose of sodium pentobarbital (50 mg/kg) via intraperitoneal injection. Animals were exsanguinated by needle stick of the hepatoportal vein until the heart stopped beating. Exsanguination was carried out with 18-23 gauge needles and blood was collected in 5-10 cc syringes for clinical chemistry analysis (**Table 1**) and complete blood count (CBC) with differential (**Table 2**). BALF and lumenal space free cells were collected using the method of Driscoll and colleagues (Driscoll *et al.*, 2000) with minor modifications. The nasal cavity and lungs were lavaged with 12 and 40 ml of 0.9% sterile saline, respectively (n=25; 5/group). The lavage fluid was centrifuged at 300g for 10 minutes to remove cellular debris and the supernatant recovered for assays. Total protein was measured as an indicator of plasma extravasation and inflammation using the method of Baughman and colleagues (1983) with bovine serum albumin (BSA) as a standard (Bicinchoninic Acid [BCA] Protein Assay Kit; Pierce, Rockford, IL). LDH was measured as an indicator of cellular integrity (CytoTox 96 Assay, Promega, Madison, WI). β-Glucuronidase was measured as an indicator of phagocytic activity, macrophage recruitment, and lysosomal injury (Bio-Rad, Hercules, CA). The protein levels and enzyme activities were determined using the Versamax microplate

automatic analyzer. The pellets containing cellular components of the lavage fluid washes were resuspended in Roswell Park Memorial Institute (RPMI) 1640 medium (Gibco, Grand Island, NY). Total cell number was determined using hemocytometry and cell viability was determined using trypan blue exclusion. Cell differentials were determined on cytocentrifuge preparations which were fixed in methanol and stained with Diff Quik (American Scientific, McGraw, IL). For each animal, 4 quadrants were viewed, and in each quadrant, 100 cells were typed.

Table 2. Endpoints Measured in the CBC with Differential **Assay**

Parameter	**Definition**
RBC	Red blood cell concentration
HGB	Hemoglobin concentration
HCT	Hematocrit (%)
MCV	Mean corpuscular volume
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
CHCM	Calculated hemoglobin concentration, mean
CH	Calculated hemoglobin
RDW	Red cell distribution width
HDW	Hemoglobin distribution width
PLT	Platelet concentration
MPV	Mean platelet volume
WBC	White blood cell concentration
%NEUT	% of neutrophils in total WBC
%LYMPH	% of lymphocytes in total WBC
%MONO	% of monocytes in total WBC
%EOS	% of eosinophils in total WBC
%BASO	% of basophils in total WBC
%LUC	% of large, unstained cells in total WBC
#NEUT	Neutrophil concentration
#LYMPH	Lymphocyte concentration
#MONO	Monocyte concentration
#EOS	Eosinophil concentration
#BASO	Basophil concentration
#LUC	Concentration of large, unstained cells

The lungs and nasal cavities from the remaining 15 animals (n=3/group) were removed for histopathological analysis. The spleens were removed from all 40 animals (n=8/group) and immune cell populations identified by flow cytometry. All other major organs were removed for histopathological analysis. The following organs/tissue groups were weighed: heart, thoracic organs (total of heart, lung and thymus), liver, kidneys, brain, sex organs, spleen and gastrointestinal tract (GI).

Harvested spleens were placed in 5 ml of complete Dulbecco's Modified Eagle Medium (DMEM) (DMEM, 10% fetal bovine serum, 0.5% penicillin-streptomycin). Cells were isolated by mincing the spleens with small scissors and then further dissociated by pressing the cells through sterile Nytex nylon mesh (Tetko, Elmsford, NY). Red blood cells were removed by hypotonic shock with distilled water for 3-5 seconds and the lymphocytes were washed thoroughly with 0.01 M phosphate-buffered saline (PBS), pH 7.4. Lymphocyte viability was determined by trypan blue exclusion. Splenocytes were diluted to 1 x 10^6 cells/ ml with PBS-NaN_3-BSA solution and stored at 4 ˚C overnight. Cells were incubated with the appropriate fluorescently tagged antibody (BD Biosciences, Franklin Lakes, NJ) for 30-60 minutes on ice. Cells were centrifuged and washed twice with 5 ml PBS-NaN_3-BSA and resuspended with 1 ml PBS-NaN_3-BSA. Antibody tagged cells were counted using a Becton-Dickinson FACScan scanning flow cytometer (Cook-Mills *et al.*, 1996). The following spleen cell phenotypes were identified: CD3 (T cells), CD4 (including, but not limited to, helper T cells), CD45RA (B cells), CD8 (cytotoxic T cells), CD161a (natural killer cells), and CD11b (neutrophils, monocytes and macrophages).

All data are reported as mean ± the standard error of the mean (SEM), unless otherwise stated. Data were analyzed using two-way analysis of variance (ANOVA), where data allowed, or one-way ANOVA for the exposed, control and naïve groups of animals with the same recovery time. If a difference among the groups was identified, Student's test was applied to identify significant differences between air-exposed controls and Jet A-exposed rats. Significance was set at $p \leq 0.05$.

Phase 2 Toxicity Study

The lack of pathological effects in the Phase 1 toxicity study differed from previously published jet fuel inhalation studies (e.g., Pfaff *et al.*, 1996); it was hypothesized that the difference was due to the use of different strains in the Pfaff studies (F344) and the Phase 1 study (Sprague-Dawley). Therefore a comparative study with both Sprague-Dawley and F344 rats was conducted. In the Phase 1 study, the activity level of the animals was also a concern. Rats are nocturnal and sleep during the day. The animals slept in the inhalation chambers during the daily 4 hour exposures. In the Phase 2 toxicity study, the circadian rhythm was adjusted by changing the light/dark cycle of the rats for the duration of the study.

Study Design and Implementation

Female Sprague-Dawley (n = 80) and F344 (n = 80) rats (7-8 weeks of age) were obtained from Charles River Laboratories. All rats underwent a 14 day quarantine/acclimation period upon arrival. On day 3 of quarantine, daily adjustments to the light/dark cycle were started. The lighting shift was increased by 1 hour/day in the morning and 1 hour/day in the evening. After 12 days, the lighting schedule was completely reversed (lights off 0600-1800; lights on 1800-0600). The rats were maintained on a reverse lighting schedule for 7 days prior to the start of the inhalation exposures and for the duration of the study. Dr. Michael Williams, Cincinnati's

Children's Hospital Research Foundation, reported that this protocol causes minimal stress on the rats and minimal changes in hormone and chemistry levels (personal communication, unpublished data).

Each group (n = 32) consisted of 16 female Sprague-Dawley rats and 16 female F344 rats. Group 1 served as naïve controls. These animals remained in the Vivarium isolated from Groups 2-5 for the entire study. Naïve controls were used due to concerns that the air control animals (Group 2) might be unintentionally exposed to background levels of Jet A. Group 2 was exposed by inhalation to filtered air. Groups 3-5 were exposed by inhalation to nominal concentrations of 500 (Group 3), 1000 (Group 4) or 2000 mg/m^3 (Group 5) of a mixed vapor/aerosol Jet A atmosphere. The animals were exposed for 4 hours/day, 7 days per week for 14 days in whole body chambers.

Inhalation exposures were conducted in the same manner as previously described for the Phase 1 toxicity study with minor adjustments. During the 14 days of inhalation exposures, the animal cages were covered while being transported from the Vivarium to the exposure chambers to prevent light exposure. The rooms where the animals were loaded and exposed to jet fuel were illuminated with red lights (which do not interfere with the rats' light-dark cycle) so the staff could navigate and run the experiment.

Study Endpoints

Twenty-four hours and 14 days following the final exposure, animals from each group (n=8/time point/strain) were euthanized by sodium pentobarbital overdose and multiple immune, pulmonary, and general toxicological endpoints were measured, as described for the Phase 1 toxicity study. The exceptions were that no rats with indwelling jugular cannulas were used, and the heart was not weighed separately (it was included with the "thoracic" organs). Additional endpoints measured in lavage fluids in the Phase 2 study were N-acteyl-β-D-glucosaminidase (NAG), chemokine (C-X-C motif) ligand 2 (CXCL2, also known as macrophage inflammatory protein 2, MIP-2), chemokine (C-C motif) ligand 2 (CCL2, also known as monocyte chemoattractant protein 1, MCP-1), interleukin 1β (IL-1β), interleukin 6 (IL-6), and tumor necrosis factor alpha (TNFα).

NAG activity was measured colorimetrically via its hydrolysis of 3-cresolsulfonphthaleinyl-N-actyl-β-D-glucosaminide to release 3-cresolsulfonphthalein (3-cresol purple) (Catalog #874 406, Roche Applied Science, Indianapolis, IN). IL-6, IL-1β, and TNFα were measured using indirect enzyme linked immunosorbent assays (Catalog #KRC0011, KRC0061, and KRC0031, respectively, Invitrogen, Carlsbad, CA).

No information was available for the methods used to measure MCP-1 and MIP-2.

RESULTS

Phase 1 Toxicity Study

Characterization of the Chamber Atmosphere

Actual chamber atmosphere concentrations achieved over the 14-days of exposure are reported in **Table 3.** Daily concentrations are reported in **Appendix A (Table 16**). The measured concentration for the low and medium concentration exposures were, on average, within 5% of target values, but the high concentration was below the targeted concentration (83.1% of target). The aerosol concentrations tended to be more variable than the vapor concentrations. There was a tendency toward increasing droplet size at higher total concentrations of jet fuel. The agreement between vapor concentrations measured by continuous IR monitoring and grab samples analyzed by GC is reported in **Table 4**.

Table 3. Characterization of Chamber Atmosphere in 14-day, Phase 1 Jet A Toxicity Study

Target concentration (mg/m^3)	Actual (total, mg/m^3, percent of target)	Vapor[a] (mg/m^3)	Aerosol (mg/m^3)	Aerosol Droplet Size	
				MMAD (µm)	σ_g
500	524.7 ± 55.7[b] (104.9%)	502.5 ± 52.0	22.2 ± 7.75	1.99 ± 0.16	2.59 ± 0.11
1000	1021 ± 96.2 (102.1%)	963.6 ± 83.0	57.0 ± 22.4	2.25 ±0.18	2.47 ±0.18
2000	1662 ± 121.5 (83.1%)	1422 ± 107	240.8 ± 31.7	2.65 ± 0.13	2.44 ± 0.09

[a] Determined by IR.

[b] Data reported as mean ± standard deviation

Table 4. Comparison of Vapor Concentrations as Determined by IR and GC

Target concentration (mg/m^3)	Vapor concentration by GC (mg/m^3)	Vapor Concentration by IR	GC/IR
500	463.5 ± 85.7	510.8 ± 21.3	90.9%
1000	731.2 ± 94.4	951.2 ± 82.7	77.7%
2000	1295 ± 169	1423 ± 60.2	91.4%

Study Endpoints

Clinical Signs, Body and Tissue Weights

No deaths or clinical signs of toxicity were observed during Jet A exposure and up to 14 days-post-exposure.

Body weights of the animals in Phase 1 of the study were presumably collected, but could not be located for analysis.

Some effects of exposure on organ weights were identified (**Table 5**). Heart weight was decreased in high-exposure group animals at all three time points (**Figure 5**). Liver weight was decreased in mid-dose animals at 24 hrs. Brain weight was increased in low dose rats at 24 hrs and in low and mid dose rats at 7 days. GI tract weight was significantly reduced in high-dose rats 14 days after the end of exposure. Organ weights may be found in Appendix A (**Table 17, Table 18, Table 19**).

Table 5. Statistically Significant Differences in Absolute Tissue Weights

Time after final exposure	Exposure Group		
	Low	**Medium**	**High**
24 hrs	↑Brain		
		↓Liver	
			↓Heart
7 days	↑Brain	↑Brain	
			↓Heart
14 days	--	--	↓Heart
			↓Gastrointestinal tract

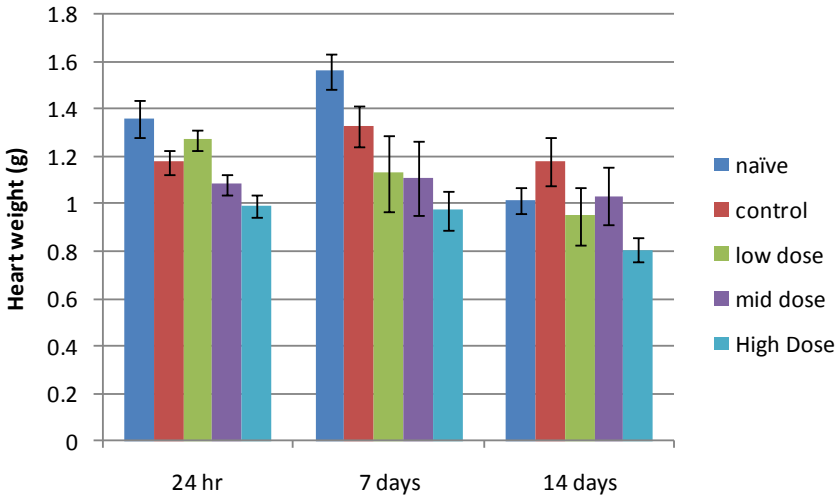

Figure 5. Heart weight of rats 24 hrs, 7 days, and 14 days after the final Jet A exposure. n= 5, except n=4 for day 7, control and high.

Hematology

Few effects of exposure on the parameters measured in the CBC were identified (**Table 6**). No significant differences were seen 24 hrs after the final exposure. At 7 days after the final exposure, the percentage of lymphocytes (percentage of total WBC) was decreased in the

medium exposure group as compared to controls. The percentage and number of eosinophils (number = concentration in plasma) were increased in the medium concentration group, relative to air exposed controls. In the high concentration group, the number of lymphocytes was decreased relative to controls. At 14 days after the end of exposure, CHCM was decreased in the low concentration group. The animal identification numbers used in the CBC reports are summarized in **Table 20**, also found in Appendix A. The individual animal CBC data may be found in Appendix A (**Table 21**, **Table 22**, and **Table 23**).

Table 6. Summary of Statistically Significant Changes in CBC Parameters

Time after final exposure	Exposure Group		
	Low	Medium	High
24 hrs	--	--	--
7 days	--	↓ %LYMPH ↑ # and %EOS	↓ #LYMPH
14 days	↓ CHCM	--	--

Clinical Chemistry

No statistically significant differences between air-exposed animals and Jet A exposed animals were found among the clinical chemistry endpoints during the exposure phase of the study. Individual animal data may be found in Appendix A (**Table 24**).

No statistically significant difference in clinical chemistry endpoints were among the exposure groups were identified during the post-exposure period. Individual animal data may be found in Appendix A (**Table 25**, **Table 26**, **Table 27**).

Lung Lavage Fluid Analyses

Lung lavage fluid analyses are summarized in **Table 7.**

Table 7. Summary of Statistically Significant Changes in Lung Lavage Fluid Parameters

Time after final exposure	Exposure Group		
	Low	Medium	High
24 hrs	--	--	--
7 days	--	↑ LDH	--
14 days	--	↑ Total Protein	--

No significant differences were detected in the lung leukocyte cell numbers (total cells or by cell type). The raw data are reported in Appendix A (**Table 28, Table 29, Table 30**).

The only statistically significant difference in total protein in the lung lavage fluid was found 14 days after the final exposure, with the total protein found to be elevated in the medium exposure

group relative to the air-exposed controls (**Figure 6**). The individual animal data may be found in Appendix A (**Table 31**).

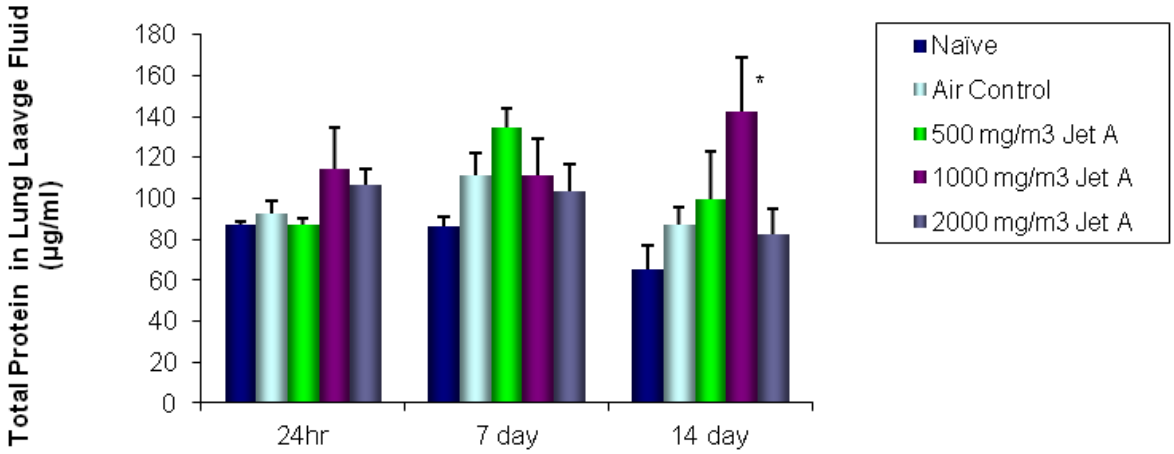

Figure 6. Concentration of total protein (µg/ml) in the lung lavage fluid 24 hrs, 7 days and 14 days following the final Jet A exposure. Asterisk denotes significant increase compared to control ($p<0.05$; $n=5$).

The only statistically significant difference in LDH in the lung lavage fluid was found 7 days after the final exposure, with LDH found to be elevated in the medium exposure group relative to the air-exposed controls (**Figure 7**). The individual animal data may be found in Appendix A (**Table 32**).

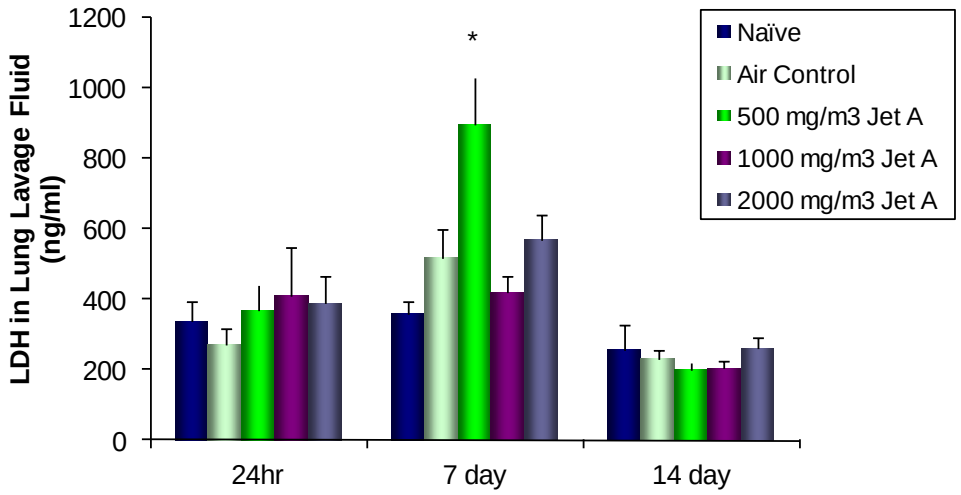

Figure 7. Concentration of lactate dehydrogenase (ng/ml) in the lung lavage fluid 24 hrs, 7 days and 14 days following the final Jet A exposure. Asterisk denotes significant increase compared to control ($p<0.05$; $n=5$).

No statistically significant differences in β-glucuronidase levels in lung lavage fluid were identified (**Figure 8**). Individual animal data are reported in Appendix A (**Table 33**).

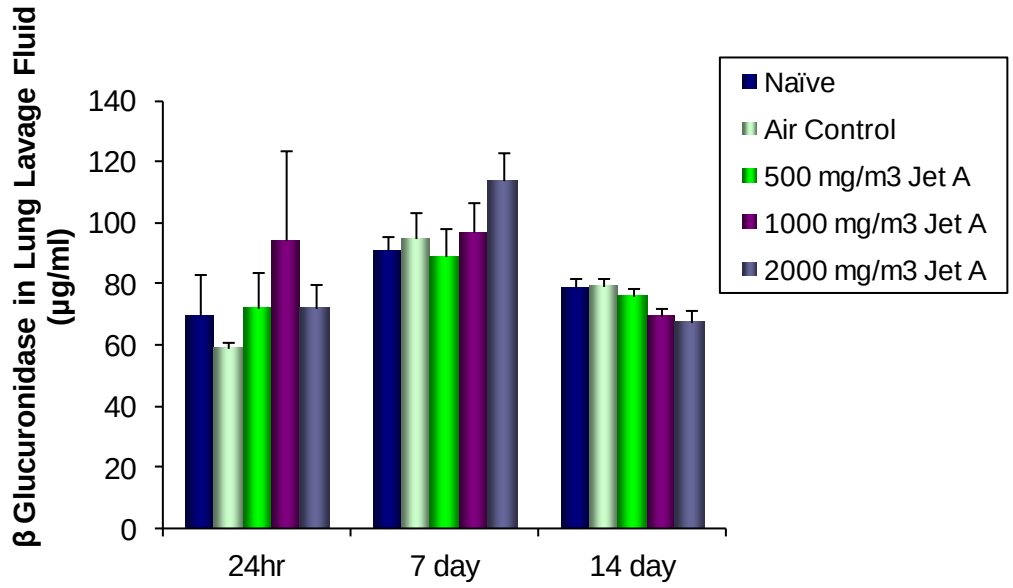

Figure 8. β-Glucuronidase in the lung lavage fluid 24 hrs, 7 days and 14 days following a 14 day exposure to jet fuel aerosol/vapor, air (control) or no exposure (naïve).

Limited indications were found suggesting toxicity to the nasal airways at high concentrations of Jet A (**Table 8**). The only statistically significant differences in total protein or LDH in the nasal lavage fluid were found 7 days after the final exposure, with both total protein and LDH found to

be elevated in the high exposure group relative to the air-exposed controls (**Figure 9** and **Figure 10**). The individual animal data may be found in Appendix A (**Table 34** and **Table 35**). No statistically significant differences in β-glucuronidase levels in nasal lavage fluid were identified (**Figure 11**). Individual animal data are reported in Appendix A (**Table 36**).

Table 8. Summary of Statistically Significant Changes in Nasal Lavage Fluid Parameters

Time after final exposure	Exposure Group		
	Low	Medium	High
24 hrs	--	--	--
7 days	--	--	↑ LDH ↑ Total Protein
14 days	--	--	--

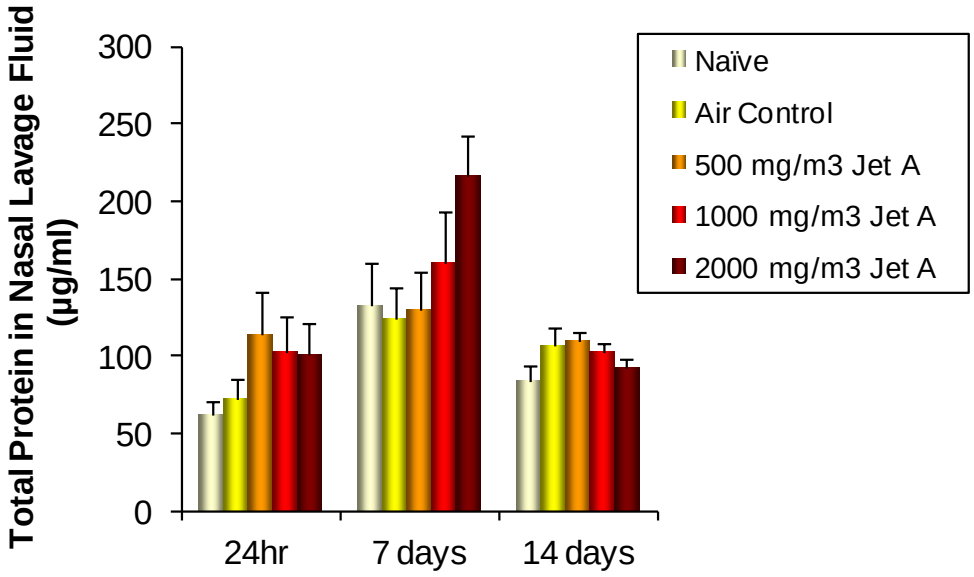

Figure 9. Concentration of total protein (µg/ml) in the nasal lavage fluid 24 hrs, 7 days and 14 days following the final Jet A exposure. Asterisk denotes significant increase compared to control ($p<0.05$; $n=5$).

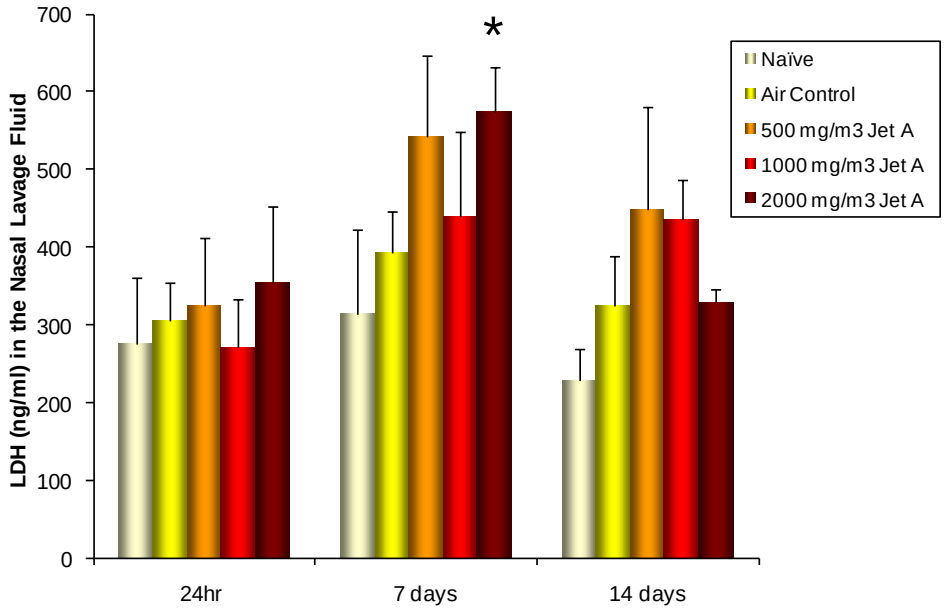

Figure 10. Concentration of lactate dehydrogenase (ng/ml) in the nasal lavage fluid 24 hrs, 7 days and 14 days following the final Jet A exposure. Asterisk denotes significant increase compared to control ($p<0.05$; $n=5$).

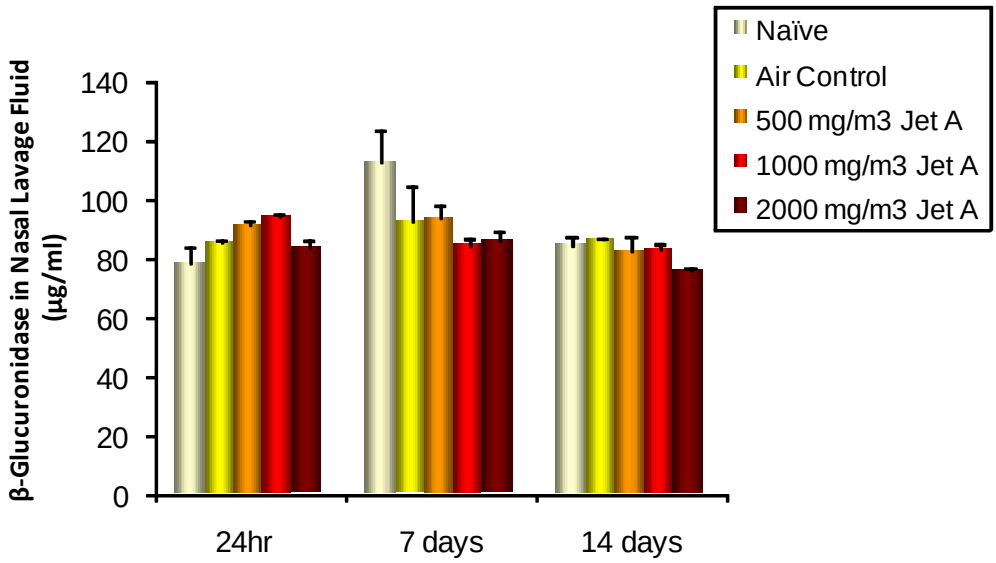

Figure 11. β-Glucuronidase in the nasal lavage fluid 24 hrs, 7 days and 14 days following a 14 day exposure to jet fuel vapor/aerosol, air (control) or no exposure (naïve)

No statistically significant differences in splenocyte populations were identified (**Figure 12, Figure 13, Figure 14, Figure 15**). Individual animal data are no longer available.

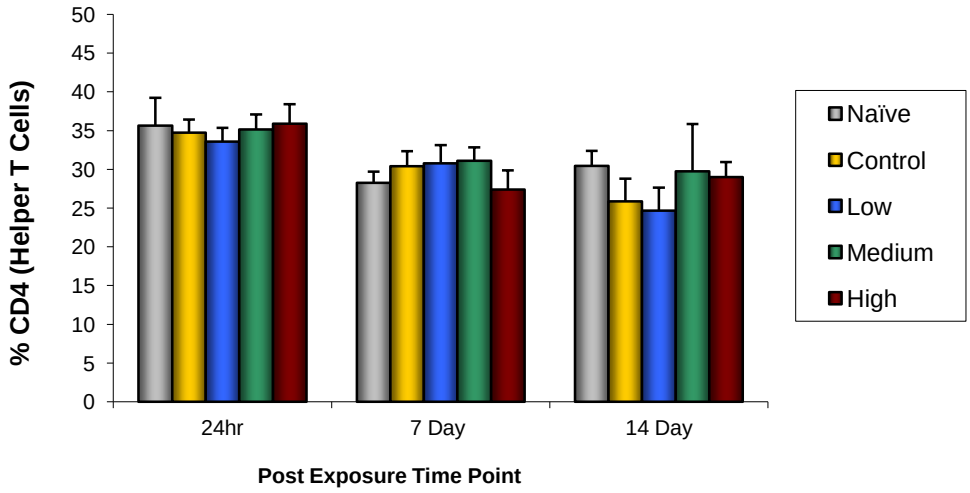

Figure 12. Percentage of CD4 (helper T cells) in the spleens 24 hrs, 7 days and 14 days after the final Jet A or air (control) exposure (n=5)

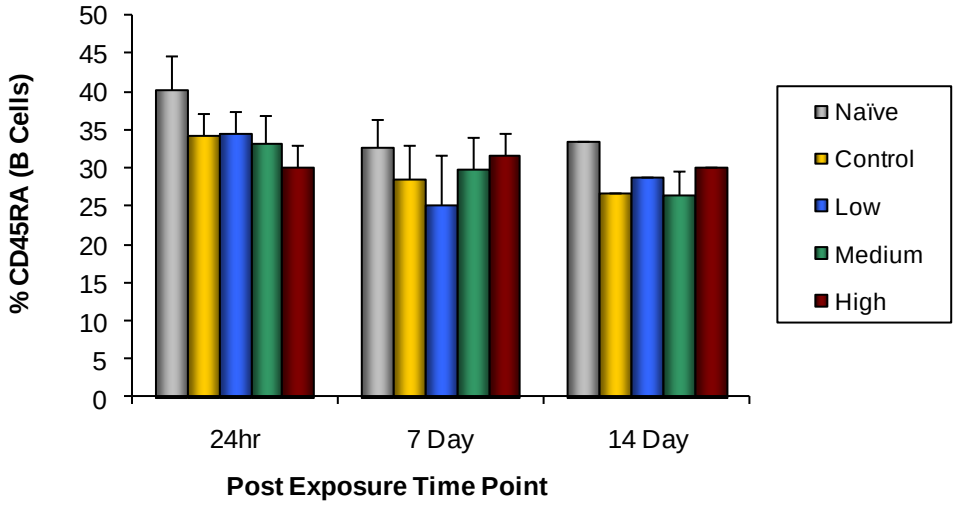

Figure 13. Percentage of CD45RA (B cells) in the spleens 24 hrs, 7 days and 14 days after the final Jet A or air (control) exposure (n= 5)

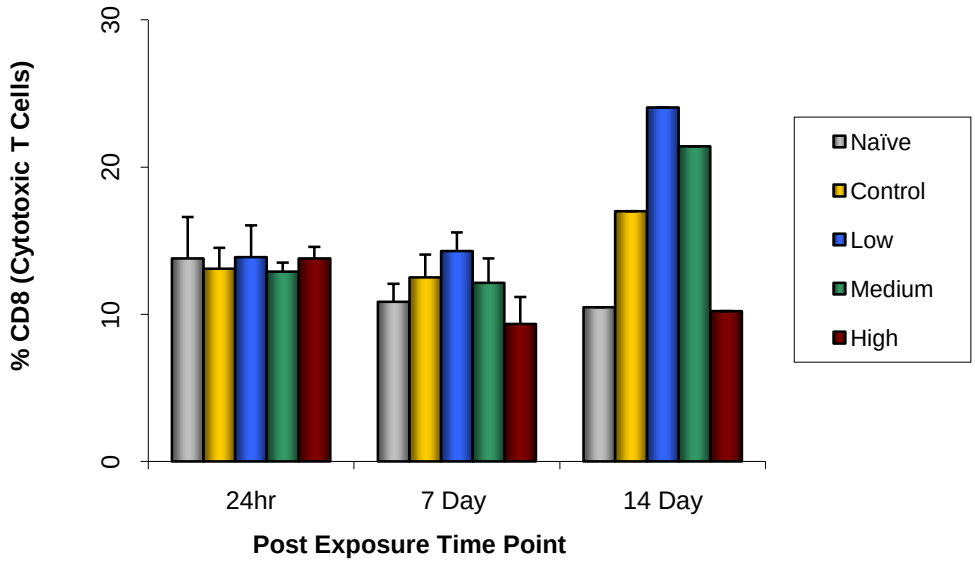

Figure 14. Percentage of CD8 (includes cytotoxic T cells) in the spleens 24 hrs, 7 days and 14 days after the final Jet A or air (control) exposure (n= 5)

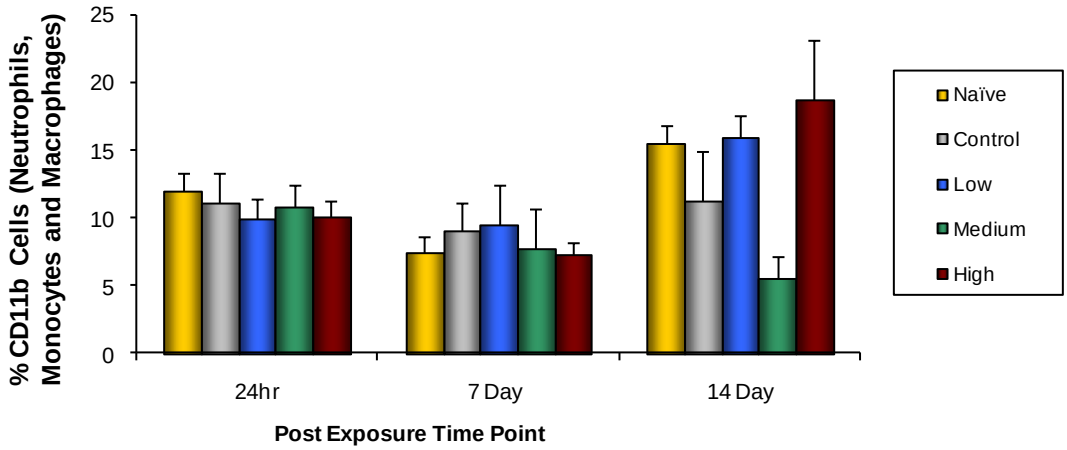

Figure 15. Percentage of CD11b (neutrophils, monocytes, and macrophages) in the spleens 24 hrs, 7 days and 14 days after the final Jet A or air (control) exposure (n=5)

Pathology

Most tissues evaluated were considered to be within normal limits. Mineralization was present within the cytoplasm of renal tubular epithelial cells in the majority of female rats evaluated histologically. Mineralization was restricted to a focally extensive region near the corticomedullary junction and in most instances was not associated with any inflammatory or other tissue reaction. Many tubular lumens within this region also contained microlithiasis (mineralized concretions). This change is found more commonly in female rats and is

considered an incidental finding usually associated with the level of hydration. Other lesions were considered incidental findings and were judged to have been clinically insignificant. There was no evidence of any infections, toxic, developmental, or neoplastic change occurring in any of the tissue sections evaluated. The summary narrative of these findings may be found at the end of Appendix A.

Summary of Phase 1 Results

This study assessed the potential airway and immune effects following subacute (14-day) Jet A exposure in female Sprague-Dawley rats. The study results are summarized in **Figures 3-13** and **Tables 5-8**. Markers of inflammation including total protein, LDH and β-glucuronidase were measured in the lungs. No dose-related inflammation was detected in the lungs 24 hrs, 7 days or 14 days following the end of 14 days of exposure to 500, 1000 or 2000 mg/m^3 of Jet-A for 4 hrs/day, when compared to controls. Exposure to 2000 mg/m^3 jet fuel may have caused significant upper airway inflammation on day 7 post-exposure, as indicated by elevated protein and LDH in nasal lavage fluid, but any inflammation resolved by day 14 post-exposure (**Figure 9** and **Figure 10, Table 8**). Markers of inflammation were not significantly elevated in the nasal cavities of rats exposed 500 or 1000 mg/m^3 compared to controls. No histological changes were observed in the lungs or nasal cavities of any of the jet fuel or air exposed animals.

Daily exposure to Jet A over a 14 day period does not appear to significantly impact lymphocyte and myloid/neutrophil cell populations in the spleens at the time points measured (**Figures 10-13**). Moreover, several clinical chemistry assays were run on the serum, and again, there were no significant differences between exposed and control animals. Few significant differences in CBC were identified (**Table 6**). The only organ weight effect that was consistently identified was a decrease in heart weight in the high exposure groups at each of the three time points evaluated (**Table 5**). Finally, the histological evaluation of the all organs examined indicated no evidence of infectious or toxic effect, and the occasional presence of inflammation or mineralization was clinically insignificant.

Overall, this study demonstrated limited evidence of effects of 14 days of exposure to Jet A on the airways of female Sprague-Dawley rats and no evidence of immunotoxicity.

Phase 2 Toxicity Study

Characterization of the Chamber Atmosphere

Actual chamber atmosphere concentrations of Jet A over the 14-days of exposure are reported in **Table 9.** Daily concentrations are reported in Appendix B **(Table 37).** The measured concentration for the low and high concentration exposures were, on average, within 9% of target values, but the medium concentration was below the targeted concentration (86.9% of target). The aerosol concentrations tended to be more variable than the vapor concentrations. There was a tendency toward increasing droplet size at higher total concentrations of jet fuel.

Table 9. Characterization of Chamber Atmosphere in 14-Day, Phase 2 Jet A Toxicity Study

Target concentration (mg/m^3)	Actual (total, mg/m^3, percent of target)	Vapor[a] (mg/m^3)	Aerosol (mg/m^3)	Aerosol Droplet Size	
				MMAD (μm)	σ_g
500	543.2 ± 48.9[b] (108.6%)	512.6 ± 36.5	30.7 ± 28.9	1.96 ± 0.54	2.98 ± 1.54
1000	869.0 ± 104.8 (86.9%)	765.1 ± 78.3	103.9 ± 32.0	2.18 ±0.11	2.32 ± 0.09
2000	1980 ± 119.3 (99.0%)	1602 ± 107	377.0 ± 66.5	2.68 ± 0.12	2.34 ± 0.13

[a] Determined by IR.

[b] Data reported as mean ± standard deviation

Observations

Based on the daily observations of the animals during the exposure, running the study under red light did not result in the animals being more active while in the inhalation chambers. While they were more active at loading and unloading times, their overall behavior when confined to the small cages within the chambers was to curl up and sleep, similar to what was observed during the previous study run under normal lighting.

Study Endpoints

Body and Organ Weights

Body weight on the last day of exposure was reduced in the F344 rats exposed to the highest concentrations, relative to all of the other groups (**Figure 16**). The weights of all of the exposed F344 rats (including those exposed to air only) were also reduced relative to the naïve F344 rats. However, by 14 days after the end of exposure, no significant differences in body weight among the groups of F344 rats were found. No significant differences in body weight on the last day of exposure or 14 days after the end of exposure were found for Sprague-Dawley rats. Individual animal identification codes and body weight data may be found in Appendix B (**Table 38, Table 39**, **Table 40, Table 41, Table 42, Table 43).**

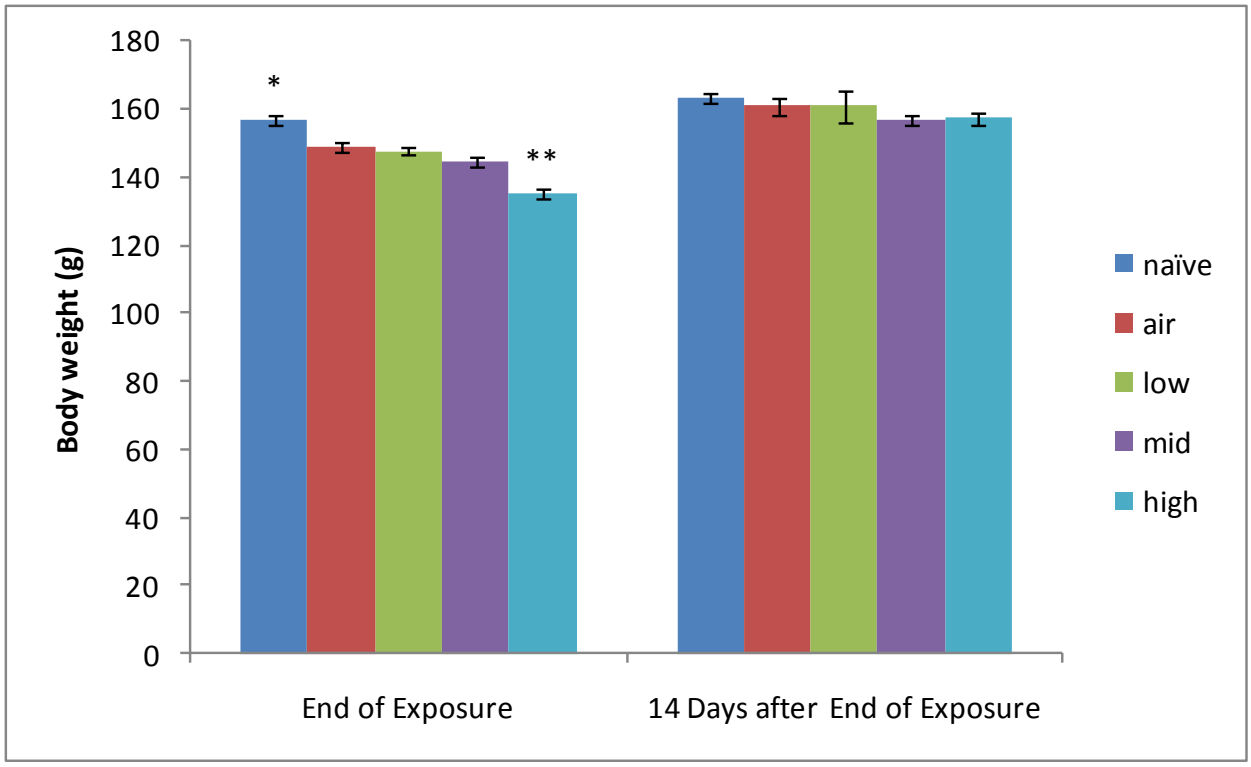

Figure 16. Body weight (mean ± SEM) of F344 rats exposed to Jet A for 14 days. * = Significantly different from air or Jet A exposed animals. ** = Significantly different from all other groups.

Few differences in organ weight (absolute or relative) were found among the groups (

Table 10). At 24 hrs after the final exposure, the absolute weight of the thoracic tissues of F344 rats in the low and medium exposure groups were significantly higher than the air-exposed controls. At 14 days after the final exposure, the only significant tissue weight differences identified were higher absolute and fractional spleen weight in the F344 medium concentration group as compared to air-exposed controls and higher fractional thoracic tissue weight in the F344 low concentration group. Individual animal tissue weight data may be found in Appendix B (**Table 44, Table 45**). The only significant tissue weight difference identified for Sprague-Dawley rats was an increased fractional liver weight at 14 days post-exposure.

Table 10. Statistically Significant Changes in Organ Weight

Time after final exposure	**F344**			**Sprague- Dawley**		
	Low	**Medium**	**High**	**Low**	**Medium**	**High**
24 hrs	↑Thoracic (absolute)	↑Thoracic (absolute)	--	--	--	--

Time after final exposure	F344			Sprague- Dawley		
	Low	Medium	High	Low	Medium	High
14 days	↑Thoracic (fractional)	↑Spleen (absolute and fraction)	--	--	--	↑Liver (fractional)

Hematology

Although differences among groups were found, evidence of dose-response relationships was generally lacking. Individual animal data may be found in Appendix B (**Table 46**, **Table 47**).

In F344 rats evaluated 24 hrs after the final exposure, CH was decreased in the low and high exposure groups and the % of neutrophils was increased in the medium exposure group, relative to air-exposed controls. At 14 days after the last exposure, the percentage of lymphocytes was increased in the high-exposure group, relative to air-exposed controls (**Table 11**).

For Sprague-Dawley rats evaluated 24 hrs after the final exposure, only one blood sample from an air-exposed control animal was available, so the statistical comparisons were made relative to naïve controls. MCV was increased in low and high exposure groups, relative to naïve animals, but was similar to the single value in an air-exposed control. CHCM was decreased in the low and high exposure groups, relative to naïve rats, but was similar to the single value for an air-exposed control. The percentage and number of basophils were increased in the low and high exposure groups, relative to naïve rats (**Figure 17**). No significant differences between air and Jet A exposed Sprague-Dawley rats were identified at 14 days after the last exposure (**Table 11**).

Table 11. Summary of Statistically Significant Changes in CBC Parameters

Time after final exposure	F344			Sprague-Dawley[a]		
	Low	Medium	High	Low	Medium	High
24 hrs	↓CH	↑%NEUT	↓CH	↑MCV ↓CHCM ↑%BASO ↑#BASO		↑MCV ↓CHCM ↑%BASO ↑#BASO
14 days	--	--	↑#LYMPH	--	--	--

[a]Exposed animals evaluated 24 hrs after the final exposure were compared to naïve animals because only one sample from an air-exposed animal was available.

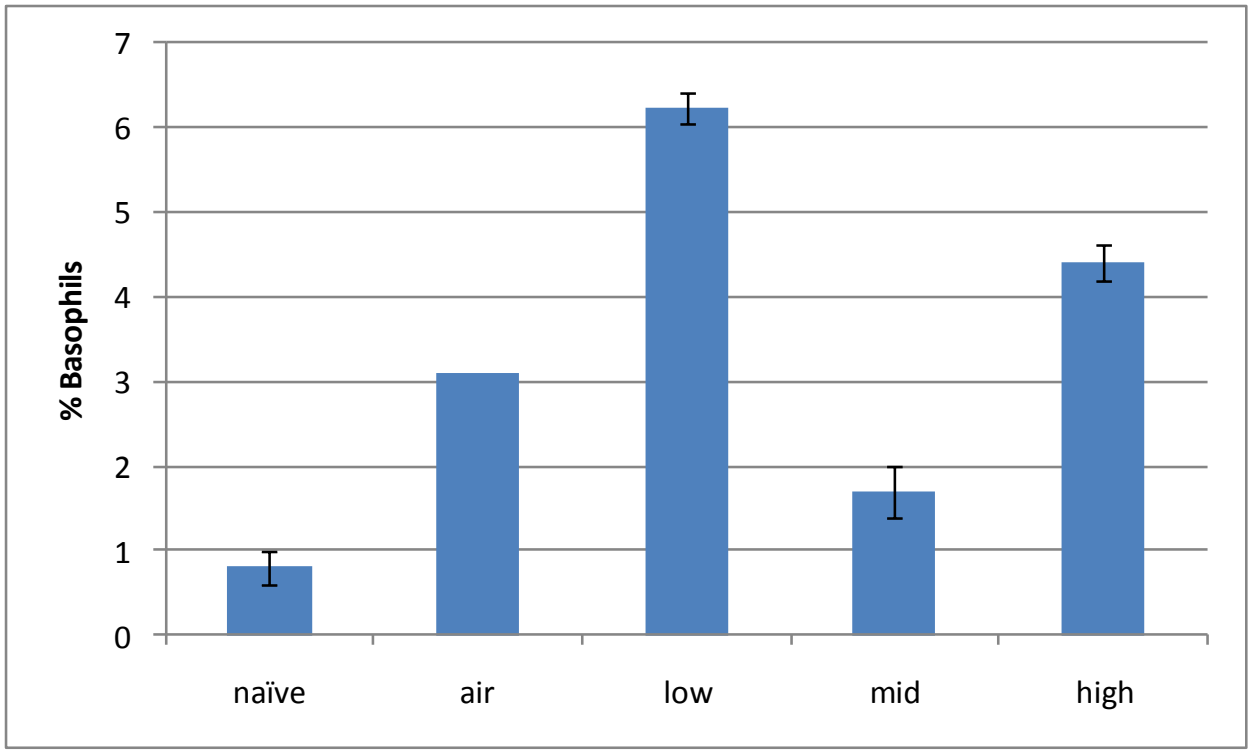

Figure 17. Percentage of basophils in the blood of female Sprague-Dawley rats 24 hrs after the final Jet A exposure. n = 2 (naive, mid), 1 (air) or 3 (low and high)

Clinical Chemistry

No significant differences in clinical chemistry parameters were observed for Jet A exposed F344 rats vs. air exposed rats of that strain at either 24 hrs or 14 days after the last exposure. For Sprague-Dawley rats, TP at 24 hrs after the final exposure was decreased in the high exposure group and appeared to be dose-related (**Figure 18**). At 14 days exposure, PHOS was elevated in the low and medium exposure groups and BUN was decreased in all exposed groups of Sprague-Dawley rats, (**Table 12**) but no dose response relationship was evident.

Table 12. Summary of Statistically Significant Changes in Clinical Chemistry Parameters

Time after final exposure	F344			Sprague-Dawley		
	Low	Medium	High	Low	Medium	High
24 hrs	--	--	--	--	--	↓TP
14 days	--	--	--	↓BUN ↑PHOS	↓BUN ↑PHOS	↓BUN

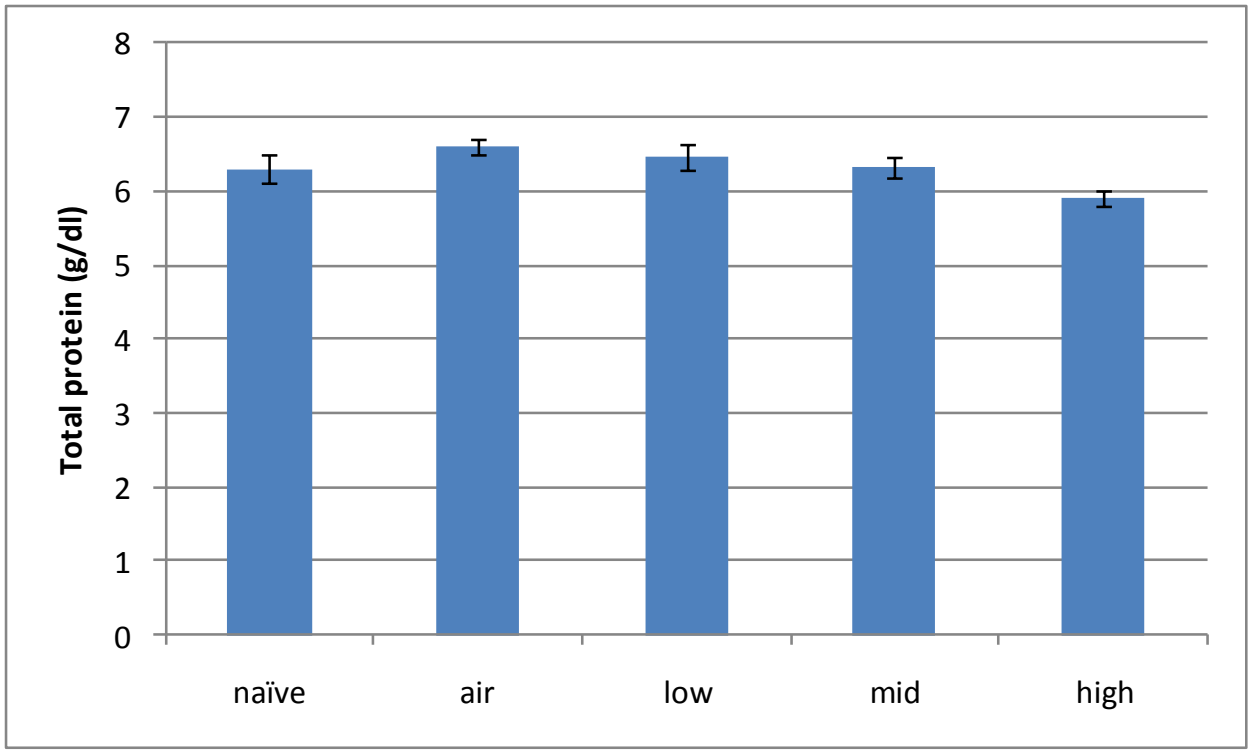

Figure 18. Total protein in the blood of female Sprague-Dawley rats 24 hrs after the final Jet A exposure (n = 5)

Lung Lavage Markers

A summary of the findings for the lung lavage data may be found in **Table 13**.

Table 13. Summary of Statistically Significant Changes in Lung Lavage Parameters

Time after final exposure	F344			Sprague-Dawley		
	Low	**Medium**	**High**	**Low**	**Medium**	**High**
24 hrs	↓NAG	↑MCP-1 ↑MIP-2	↓NAG ↑MCP-1 ↑MIP-2	↓NAG ↑MCP-1 ↑Total Protein	↑Total Protein	↑MCP-1 ↑Total Protein
14 days	↑LDH	↑Total Protein	↓MIP-2	--	↑LDH ↑Total Protein ↑NAG	↑MCP-1

No significant differences were detected in the lung leukocyte cell populations expressed as percent of each cell type (total numbers of cells were not available). The individual animal data are reported in Appendix B (**Table 48**, **Table 49**).

At 24 hrs after the last exposure, there were no significant differences in total protein in lung lavage fluid between air controls and exposed F344 rats. At the same time, all exposed groups of Sprague-Dawley rats had modestly elevated levels of total protein without evidence of a consistent dose-response relation. At 14 days after the last exposure, total protein was elevated in the medium groups of each strain, relative to their respective air-exposed controls. Individual animal data may be found in Appendix B (**Table 50, Table 51**).

No effect on LDH levels in lung lavage fluid in either strain was observed at 24 hrs after the last exposure. When measured 14 days after the final exposure, LDH levels were elevated in the low exposure group of F344 rats and the medium exposure group of Sprague-Dawley rats. Individual animal data may be found in Appendix B **(Table 52, Table 53**).

NAG was depressed in F344 rats in the low and high exposure groups 24 hrs after the final exposure and in the Sprague-Dawley rat low exposure group. At 14 days post-exposure, no statistically significant differences between exposed groups and air-exposed controls were noted for F344 rats. Among Sprague-Dawley rats, NAG was elevated in the medium exposure group, when compared to the air-exposed controls. Individual animal data may be found in Appendix B **(Table 54, Table 55**).

No significant differences in β-glucuronidase were noted for F344 or Sprague-Dawley rats at 24 hrs or 14 days after the final exposure. Individual animal data may be found in Appendix B (**Table 56, Table 57**).

MCP-1 was elevated at 24 hrs after the final exposure in F344 rats exposed to medium and high concentrations of Jet A and Sprague-Dawley rats exposed to low or high concentrations. At 14 days after the final exposure, no MCP-1 measurements were made for the low and medium exposure groups. At the high Jet A exposure, MCP-1 was elevated in Sprague-Dawley rats, but not F344 rats (**Figure 19**). Individual animal data may be found in Appendix B (**Table 56, Table 57**).

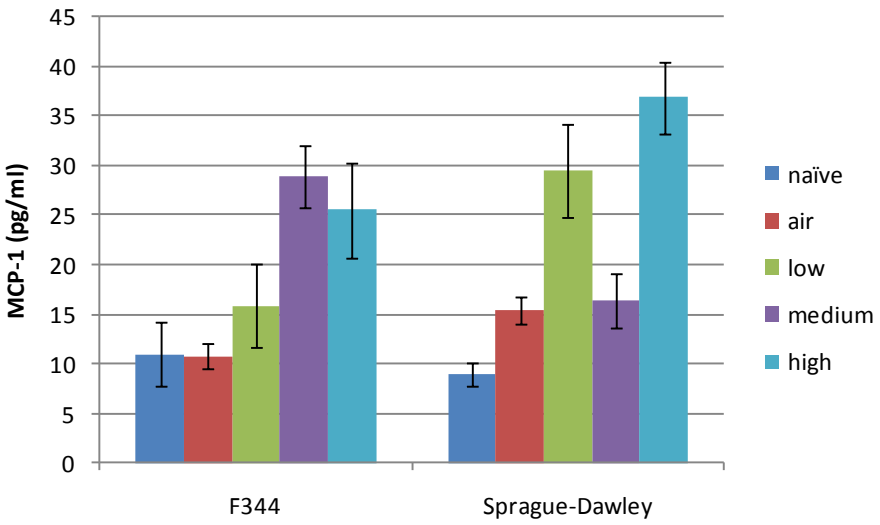

Figure 19. MCP-1 in lung lavage fluid 24 hrs after the final Jet A exposure (n= 5, except n=3 for the F344 and Sprague-Dawley medium concentration groups)

MIP-2 was elevated at 24 hrs after the final exposure in F344 rats exposed to medium and high concentrations of Jet A (**Figure 20**). At 14 days after the final exposure, MIP-2 was decreased in the high exposure F344 group. No differences were noted between air and Jet A exposed Sprague-Dawley rats at 24 hrs or 14 days after the final exposure (data not shown). Individual animal data may be found in Appendix B (**Table 56, Table 57**).

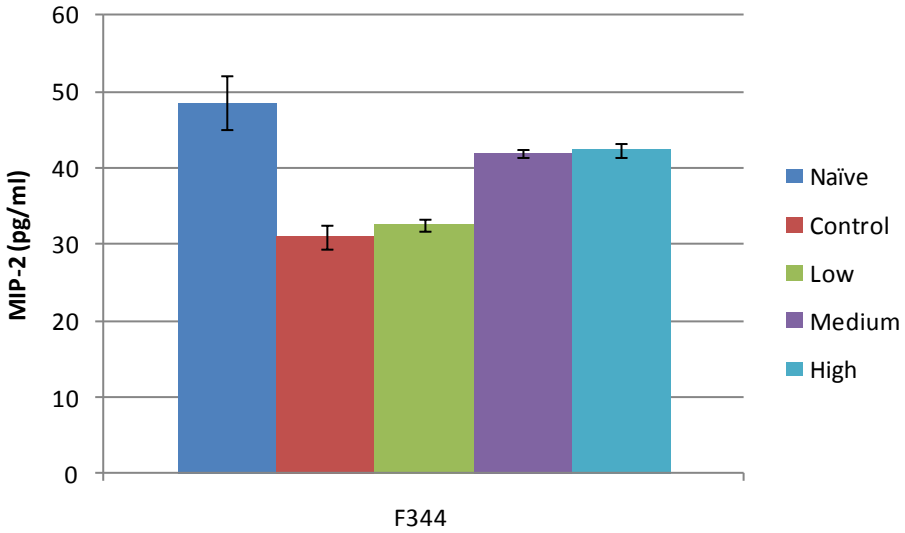

Figure 20. MIP-2 in lung lavage fluid 24 hrs after the final Jet A exposure (n = 5)

IL-1β, IL-6, and TNFα were assayed only in the lung lavage fluid of rats exposed to high concentrations of Jet A. The results consisted primarily of negative values and were highly variable, so these data were not used.

Nasal Lavage Fluid

Nasal lavage fluid data are summarized in **Table 14**.

Table 14. Summary of Statistically Significant Changes in Nasal Lavage Parameters

Time after final exposure	F344			Sprague-Dawley		
	Low	**Medium**	**High**	**Low**	**Medium**	**High**
24 hrs	--	--	--	--	--	--
14 days	--	↓LDH	↓Total Protein	--	↑β-glucuronidase	↑β-glucuronidase ↑MCP-1

At 24 hrs after the last exposure, no statistically significant differences between Jet A-exposed rats or air-exposed controls were identified for any assayed nasal lavage parameter (total protein, LDH, NAG, β-glucuronidase, MIP-2 or MCP-1). Individual animal data may be found in Appendix B (**Table 58**).

At 14 days after the final exposure, total protein in nasal lavage fluid was reduced in F344 rats in the high exposure group, but no significant differences were noted for Sprague-Dawley rats. At 14 days after exposure, nasal lavage fluid LDH was significantly lower in the medium exposure group of F344 rats than in air-exposed controls; no differences between control and exposed Sprague-Dawley rats were noted at that time. No statistically significant differences in NAG in nasal lavage fluid from Jet A exposed and control animals were noted. At 14 days after exposure, β-glucuronidase was significantly increased in F344 rats exposed to medium or high concentrations of Jet A, but no differences were found among the Sprague-Dawley rats. MIP-2 was measured only in nasal lavage fluid from rats exposed to the high concentration of Jet A and air-exposed controls. No statistically significant differences were identified. MCP-1 was measured only in nasal lavage fluid from rats exposed to the high concentration of Jet A and air-exposed controls. At 14 days after the end of exposure, MCP-1 was significantly increased in Sprague-Dawley rats, but not F344 rats, exposed to high concentrations of Jet A. IL-1β was assayed only in the nasal lavage fluid of rats exposed to high concentrations of Jet A and air-exposed controls. The data consisted primarily of negative values and were highly variable, so the dataset was not used. Individual animal data measured 14 days after the final exposure may also be found in Appendix B (**Table 59**).

Spleen Cell Phenotypes

The following statistically significant changes in splenocyte surface marker expression were identified in F344 rats at 24 hrs after the last exposure: decreased CD3 and increased CD161a in the medium exposure group and decreased CD45RA in the high exposure group. At 14 days, increased CD3 was observed in the low exposure group and decreased CD161a was observed in the medium exposure group (**Table 15)**.

No changes in splenocyte surface markers were found in Sprague-Dawley rats evaluated 24 hrs after the final exposure. At 14 days after the final exposure, the percentage of CD161a cells decreased in the medium exposure group and expression of CD 4 increased in the low and medium exposure groups (**Table 15**).

Table 15. Summary of Statistically Significant Changes in Spleen Cell Phenotypes

Time after final exposure	F344			Sprague-Dawley		
	Low	**Medium**	**High**	**Low**	**Medium**	**High**
24 hrs	--	↓CD3 ↑CD161a	↑CD45RA	--	--	--
14 days	↑CD3	--	↓CD161a	↑CD4	↓CD161a ↑CD4	

Pathology

There was no evidence of infections, toxic, developmental, or neoplastic change/transformation occurring in any of the tissue sections evaluated. Various lesions of minimal to mild severity were identified, but the frequency and dose distribution were judged to be consistent with historical findings for these strains, incidental findings, or tissue handling artifacts and not related to test article administration. These lesions included minimal to mild subacute inflammation within the liver, mineralization within renal tubules, possible early manifestations of chronic progressive nephropathy, and histiocytic alveolar infiltrates. Edema of separating smooth muscle fibers and lymphangiectasia were seen within the uterine myometrium. The narrative pathology summary report can be found at the end of Appendix B.

Summary of Phase 2 Results

This study assessed the potential airway and immune effects following subacute (14-day) jet fuel exposure in female F344 and Sprague-Dawley rats and allowed for comparisons of the sensitivity of the two strains. The study results are summarized in **Figure 16-Figure 20** and

Table 10-**Table 15**. After the last exposure, body weights of the F344 rats in the high exposure group were depressed, as compared to the controls. No effect on body weight was observed in

Sprague-Dawley rats. Few organ weight changes were noted for either strain. Likewise, no apparent dose-related changes in CBC or spleen cell phenotype were noted. Among clinical chemistry parameters, a statistically significant decline in total blood protein was noted, and appeared to be dose related. Some lung lavage fluid markers were increased at 24 hrs after the final exposure, indicating possible airway injury/inflammation. However, no test article histological changes were observed in the lungs, nasal cavities, or any other tissue of any of the jet fuel exposed animals. Overall, this study demonstrated limited evidence of effects of 14 days of exposure to Jet A on the airways, immune system, or any other organ or system of female Sprague-Dawley and F344 rats.

DISCUSSION

While many endpoints have been measured to look at the pulmonary toxicology and immunotoxicology of jet fuels, the comparisons presented here will be limited to endpoints that are equivalent or comparable to those investigated in the current 14-day studies of female Sprague-Dawley and F344 rats.

Four weeks of unoccluded dermal exposure of female Sprague-Dawley rats to Jet A (165, 330, or 495 mg/kg/d) did not alter body weight and did not alter the absolute or relative weight of the spleen or the thymus. Likewise, the number and percentage of CD45+, CD5+ (total T cells), CD4+CD5+ (T helper), and CD8+CD5+ (cytotoxic T cells) cells were not altered at any tested dose (Mann *et al.*, 2008). Based on the alveolar ventilation rate for rats provided by Brown *et al.* (1997), the ~150-g rats in the current study would breathe ~4.8 L/hr. Given a 4 hr exposure to nominal concentrations of 500, 1000, and 2000 mg/m^3, the expected administered dose is approximately 64, 127, or 254 mg/kg/d, of which not all is absorbed. Thus the current study utilizes at least one dosing level that is within the range of the Mann *et al.* (2008) study, which used the same strain and sex of rats as in both the current Phase 1 and Phase 2 toxicity studies as well as the same type of fuel. The results are consistent in that this strain did not show altered body weight, altered immune tissue weight, or changes in spleen cell phenotypes.

Rossi *et al.* (2001) exposed male Sprague-Dawley rats to JP-5 (1200 mg/m^3 vapor) or JP-8 (1000 mg/m^3 vapor) for 6 hours/day, 5 days/week for 6 weeks. No changes in body weight or body weight gain were observed in the exposed groups, consistent with the findings in the current 14-day study. In male Sprague-Dawley rats exposed to 1000 mg/m^3 JP-8 for 6 hrs/day for 91 days, a 5% weight loss was observed, with animals exposed to 500 mg/m^3 showing no change in body weight (Hanas *et al.*, 2010). Thus while body weight gain may be a concern for jet fuel exposed rats, extended and/or elevated exposure durations may be required to produce an effect.

Pfaff *et al.* (1995) exposed male F344 rats, for 1 hr/day, for 7 or 28 days to approximately 500 mg/m^3 JP-8 aerosol plus an unreported level of vapor phase JP-8 in a nose-only system. An aerosol/vapor ratio of 1.2-1.8 was subsequently reported (Pfaff *et al.*, 1996). Both exposed groups had significantly less weight gain than their longitudinal controls (sham exposure). In the current 14 day study with female F344 rats, significantly lower body weight was observed only at 2000 mg/m^{3}and not 1000 mg/m^3 (total) Jet A. Pfaff *et al.* (1996) report additional data on the rats exposed as described above plus "high dose" rats (814 mg/m^3 aerosol for 7 days or 1094 mg/m^3 for 28 days). Body weight changes for the high dose groups were not reported. Pathological changes to the lungs were reported for all JP-8 exposed rats in their study. The following changes were seen: 7 day low dose - thickened epithelium in terminal bronchioles; 7 day high dose - widespread pulmonary congestion with hemorrhaging in the distal lung; both 28 day groups - local accumulations of inflammatory cells around terminal bronchioles and

degeneration of alveolar type II cells, edema, an influx of leukocytes, swelling of terminal bronchial airways, and scattered disruption of the epithelial layer. Hays *et al.* (1995) reported additional information on BALf from these groups and groups exposed for 56 days. Total cells in BALf were elevated in the high dose group after 7 days of exposure, but not after 28 days exposure. At 56 days, the total number of cells in BALf was reduced in both the low and high-dose groups, relative to controls. The only instance in which the BALf differential was altered was an elevation of the % granulocytes in the low dose 7-day group as compared to the high dose 7-day group (but not the longitudinal controls). Thus the most notable responses in these studies were the histopathology. Based on the average reported aerosol/vapor ratio of 1.5 (Pfaff *et al.*, 1996), the "low" exposures were equivalent to approximately 833 mg/m^3, which is still less than the highest concentration in the current study, and with a shorter daily duration (1 hr vs. 4 hrs). Their aerosol/vapor ratio of ~1.5 is very different from what was found in this study (e.g., 57/963 = 0.059 at the medium dose in Phase 1, 104/765 = 0.14 at the medium dose in Phase 2), although it should be noted that different generating systems were used. Thus it is unclear why Witten and co-workers observed extensive lung damage (Pfaff *et al.*, 1995, 1996, Hays *et al.*, 1995), while no such damage was found in the current "Phase 2" study, which utilized the same strain (but a different sex) of rats and a negligibly different fuel. The uncertainty regarding the exposure atmosphere in the studies of Witten and co-workers (Tremblay *et al.*, 2010) suggests that the difference may be due to greater exposure intensities in their studies.

CONCLUSIONS

The Phase 1 study assessed the potential airway and immune effects following subacute (14-day) exposures of female Sprague-Dawley rats to 500, 1000 or 2000 mg/m^3 of Jet-A for 4 hrs/day. Markers of inflammatory including total protein, LDH and β-glucuronidase were measured in the lungs. No dose-related inflammation was detected in the lungs 24 hrs, 7 days or 14 days following the end of 14 days of exposure, when compared to controls. Exposure to 2000 mg/m^3 jet fuel may have caused significant upper airway (nasal) inflammation on day 7 post-exposure, as indicated by elevated protein and LDH in nasal lavage fluid, but any inflammation resolved by day 14 post-exposure. Markers of inflammation were not significantly elevated in the nasal cavities of rats exposed 500 or 1000 mg/m^3 compared to controls. Daily exposure to Jet A over a 14 day period does not appear to significantly impact lymphocyte and myloid/neutrophil cell populations in the spleens at the time points measured. Moreover, several clinical chemistry assays were run on the serum, and again, there were no significant differences between exposed and control animals. Few significant differences in CBC were identified. The only organ weight effect that was consistently identified was a decrease in heart weight in the high exposure. Finally, the histological report of the all organs examined showed no evidence of infectious or toxic effect, and the occasional presence inflammation or mineralization was clinically insignificant. Overall, this study demonstrated limited evidence of effects of 14 days of exposure to Jet A on the airways of female Sprague-Dawley rats and no evidence of immunotoxicity.

The Phase 2 study assessed the potential airway and immune effects following subacute (14-day) jet fuel exposure in female F344 and Sprague-Dawley rats and allowed for comparisons of the sensitivity of the two strains. The study design (exposure concentrations, endpoints, etc.) differed only minimally from the Phase 1 study. After the last exposure, body weights of the F344 rats in the high exposure group were depressed, as compared to the controls. No effect on body weight was observed in Sprague-Dawley rats. Few organ weight changes were noted for either strain. Likewise, no apparent dose-related changes in CBC or spleen cell phenotype were noted. Among clinical chemistry parameters, a statistically significant decline in total blood protein was noted, and appeared to be dose related. Some lung lavage fluid markers were increased at 24 hrs after the final exposure in each strain, indicating possible airway injury/inflammation. However, no test article histological changes were observed in the lungs, nasal cavities, or any other tissue of any of the jet fuel exposed animals. Overall, this study demonstrated limited evidence of effects of 14 days of exposure to Jet A on the airways, immune system, or any other organ or system of female Sprague-Dawley and F344 rats, with no remarkable differences between strains.

While the results of the studies described herein were similar to other investigations of jet fuel toxicity in rats with respect to some endpoints (body and organ weights), there were differences with respect to observations of lung pathology (Hays *et al.*, 1995; Pfaff *et al.*, 1995, 1996).

While it is possible that the differences in outcome are due to differences in gender and jet fuel composition, a difference in total exposure concentration (vapor plus aerosol, Tremblay *et al.*, 2010) appears to be the most plausible explanation for the differences among these studies.

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APPENDIX A

Supporting Documentation for Phase 1 Toxicity Study

Exposure Characterization

Table 16. Chamber Concentrations (mg/m^3)

	Low Chamber					Medium Chamber				
Day			***Chamber Aerosol***		***Total***			***Chamber Aerosol***		***Total***
#	***mmad***[a]	σ_g	***conc***	***conc***	***conc***	***mmad***	σ_g	***conc***	***conc***	***conc***
1	1.91	2.52	497.50	13.14	510.64	2.26	2.54	830.50	35.48	865.98
1	2.05	2.67	496.50	15.92	512.42	2.06	2.46	854.50	47.52	902.02
2	2.13	2.78	538.50	12.72	551.22	2.61	2.35	905.50	35.22	940.72
2	1.72	2.54	514.50	20.54	535.04	2.10	2.43	877.50	53.06	930.56
3	1.86	2.68	488.50	14.93	503.43	2.10	2.45	869.50	51.26	920.76
3	1.87	2.62	488.50	19.57	508.07	2.27	2.56	909.50	58.59	968.09
4	1.60	2.37	504.50	17.21	521.71	2.25	2.52	900.50	26.13	926.63
4	1.85	2.64	521.50	22.08	543.58	2.15	2.51	892.50	26.50	919.00
5	2.04	2.64	534.50	14.03	548.53	2.25	2.46	1060.50	49.22	1109.72
5	1.90	2.57	512.50	20.46	532.96	2.13	2.43	958.50	56.76	1015.26
6	2.07	2.72	327.50	8.54	336.04	2.23	2.38	888.50	61.39	949.89
6	2.23	2.68	337.50	17.04	354.54	2.20	2.40	960.50	65.07	1025.57
7	2.07	2.62	497.50	26.49	523.99	2.44	2.47	933.50	48.87	982.37
7	2.12	2.53	539.50	6.39	545.89	2.42	2.51	945.50	48.85	994.35
8	2.27	2.76	524.50	27.72	552.22	2.37	2.42	1100.50	107.77	1208.27
8	1.94	2.62	522.50	27.30	549.80	2.41	2.35	1143.50	98.75	1242.25
9	1.95	2.64	483.50	18.04	501.54	2.17	2.42	1088.50	90.57	1179.07
9	2.01	2.63	468.50	24.63	493.13	2.29	2.38	1100.50	6.33	1106.83
10	2.15	2.30	501.50	25.43	526.93	2.31	2.40	886.50	53.10	939.60
10	1.87	2.56	537.50	30.01	567.51	2.24	2.26	963.50	57.27	1020.77
11	2.01	2.67	510.50	25.13	535.63	2.65	2.55	1027.50	49.74	1077.24
11	1.90	2.45	541.50	35.24	576.74	2.27	2.51	1010.50	54.86	1065.36
12	1.78	2.68	528.50	31.02	559.52	2.22	2.65	902.50	45.52	948.02
12	1.90	2.71	549.50	31.27	580.77	2.19	2.48	958.50	52.09	1010.59
13	2.07	2.45	514.50	31.54	546.04	1.65	3.32	1001.50	74.93	1076.43
13	2.29	2.50	532.50	31.43	563.93	2.28	2.38	1028.50	80.67	1109.17
14	2.03	2.47	523.50	21.43	544.93	2.32	2.31	991.50	74.22	1065.72
14	2.08	2.63	532.50	32.60	565.10	2.29	2.39	990.50	85.65	1076.15
Average	**1.99**	**2.59**	**502.50**	**22.21**	**524.71**	**2.25**	**2.47**	**963.61**	**56.98**	**1020.59**
Std. Deviation	**0.16**	**0.11**	**52.04**	**7.75**	**55.73**	**0.18**	**0.18**	**83.02**	**22.35**	**96.15**
Precision	**0.08**	**0.04**	**0.10**	**0.35**	**0.11**	**0.08**	**0.07**	**0.09**	**0.39**	**0.09**

[a]**MMAD in µm**

Table 16. Chamber Concentrations (mg/m3)** Cont'd

	High Chamber				
Day			***Chamber Aerosol***		***Total***
#	***mmad***	σ_g	***conc***	***conc***	***conc***
1	2.70	2.37	1398.00	198.10	1596.10

High Chamber					
Day			***Chamber***	***Aerosol***	***Total***
#	***mmad***	σ_g	***conc***	***conc***	***conc***
1	2.67	2.37	1833.00	247.25	2080.25
2	2.72	2.45	1351.00	204.26	1555.26
2	2.65	2.40	1414.00	281.24	1695.24
3	2.79	2.48	1358.00	219.93	1577.93
3	2.72	2.35	1498.00	264.12	1762.12
4	2.72	2.44	1334.00	223.40	1557.40
4	2.63	2.43	1439.00	253.97	1692.97
5	2.76	2.49	1418.00	212.96	1630.96
5	2.84	2.42	1509.00	322.45	1831.45
6	2.57	2.43	1293.00	242.56	1535.56
6	2.83	2.58	1482.00	270.09	1752.09
7	2.83	2.56	1337.00	221.22	1558.22
7	2.68	2.45	1460.00	264.88	1724.88
8	2.72	2.45	1354.00	224.66	1578.66
8	2.60	2.44	1485.00	254.00	1739.00
9	2.70	2.31	1375.00	215.38	1590.38
9	2.59	2.41	1460.00	257.39	1717.39
10	2.57	2.43	1326.00	226.98	1552.98
10	2.62	2.39	1486.00	266.69	1752.69
11	2.58	2.40	1348.00	243.43	1591.43
11	2.65	2.42	1486.00	266.65	1752.65
12	2.26	2.80	1316.00	220.58	1536.58
12			1518.00	240.08	1758.08
13	2.45	2.49	1334.00	230.61	1564.61
13	2.73	2.34	1447.00	269.61	1716.61
14	2.50	2.40	1306.00	244.01	1550.01
14	2.50	2.38	1437.00	154.99	1591.99
Average	**2.65**	**2.44**	**1421.50**	**240.77**	**1662.27**
Std. Deviation	**0.13**	**0.09**	**106.57**	**31.72**	**121.49**
Precision	**0.05**	**0.04**	**0.07**	**0.13**	**0.07**

Organ Weights

Table 17. Organ Weights, Measured 24 hrs after the Final Exposure

Heart

High Dose		*Mid Dose*		*Low Dose*[b]		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
97	0.99	65	1.1	33	1.06	201	1.06	129	1.45
98	1	66	1.2	34	1.56	202	1.25	130	1.07
99	0.93	67	1.1	35	0.93	203	1.08	131	1.5
100	1.16	68	1.09	36	1.09	204	1.18	132	1.29
101	0.89	69	0.93	37	1.71	205	1.32	133	1.49

Thoracic (Heart lungs thymus)

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)

102	3.61	70	4.27	38	3.7	206	3.84	134	4.18
103	4.23	71	4.45	39	3.41	207	4.73	135	4.85
104	3.13	72	4.04	40	4.32	208	4.02	136	4.08

Liver

High Dose[a]		*Mid Dose*[a]		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
97	10.34	65	11.05	33	10.86	201	14.3	129	12.98
98	9.91	66	10.9	34	12.86	202	11.52	130	10.93
99	10.52	67	10.61	35	12.51	203	11.67	131	12.88
100	11.34	68	10.73	36	11.22	204	13.31	132	13.12
101	10.54	69	11.87	37	11.18	205	10.3	133	15.09
102	12.24	70	11.5	38	10.26	206	11.96	134	11.91
103	12.95	71	10.01	39	10.95	207	11.29	135	12.05
104	9.05	72	10.51	40	13.76	208	13.45	136	14.21

Kidneys

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
97	1.88	65	1.96	33	1.98	201	2.01	129	2.15
98	1.93	66	2.23	34	2.43	202	2.1	130	1.98
99	1.81	67	2.07	35	2.01	203	1.95	131	2.32
100	2.03	68	1.94	36	2.01	204	2.21	132	2.55
101	1.97	69	2.05	37	2.06	205	2.06	133	2.19
102	2.19	70	2.29	38	2.46	206	2.32	134	2.53
103	2.26	71	2.51	39	2.22	207	2.34	135	2.32
104	1.79	72	1.94	40	2.78	208	2.21	136	2.23

Brain

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
97	1.89	65	1.96	33	1.96	201	1.66	129	1.78
98	1.88	66	2	34	1.86	202	1.69	130	1.65
99	1.58	67	1.74	35	2.07	203	1.78	131	1.77
100	1.79	68	1.91	36	1.98	204	1.88	132	1.66
101	1.92	69	1.79	37	1.9	205	1.69	133	1.75
102	1.7	70	1.82	38	1.98	206	1.87	134	0.86
103	2.48	71	1.95	39	1.89	207	1.91	135	1.97
104	1.65	72	1.93	40	1.84	208	1.88	136	1.36

Spleen

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
97	0.66	65	0.51	33	0.68	201	0.7	129	0.76
98	0.42	66	0.66	34	0.79	202	0.78	130	0.51
99	0.68	67	0.69	35	0.78	203	0.72	131	0.68
100	0.66	68	0.65	36	0.6	204	0.57	132	0.8
101	0.72	69	0.65	37	0.55	205	0.6	133	0.6
102	1.06	70	0.8	38	0.7	206	0.81	134	0.75

103	0.59	71	0.67	39	0.56	207	0.74	135	0.67
104	0.62	72	0.5	40	0.74	208	0.84	136	0.82

GI Tract

High Dose[a]		*Mid Dose*[a]		*Low Dose*		*Control*[a]		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
97	23.4	65	22.41	33	24.34	201	25.08	129	34.34
98	21.3	66	23.14	34	29.82	202	25.82	130	27.91
99	26.94	67	24.11	35	27.68	203	22.83	131	31.74
100	25.16	68	23.53	36	25.07	204	27.46	132	38.15
101	21.79	69	25.38	37		205		133	34.88
102	25.13	70	24.97	38	25.11	206	30.32	134	28.23
103	24.98	71	26.35	39	27.42	207	32.8	135	28.42
104	22.27	72	20.94	40	32.92	208	22.99	136	32.35

[a]Different from naïve ($p<0.05$)

[b]Different from control ($p<0.05$)

Table 18. Organ Weights, Measured 7 days after the Final Exposure

Heart

High Dose [a, b.]		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
105		73	1.11	41	1.47	209	1.19	137	1.83
106	1.12	74	0.9	42	1.2	210	1.38	138	1.44
107	0.8	75	1.04	43	1.21	211		140	1.59
108	1.11	76	1.71	44	0.83	212	1.2	141	1.52
109	0.86	77	0.79	45	0.94	213	1.55	142	1.42

Thoracic (Heart lungs thymus)

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
110	3.85	78	4.15	227	4.49	214	3.88	143	4.59
111	4.29	79	4.44	47	4.98	215	4.33	144	4.14
112	4.27	80	4.66	48	4.31	216	5.08	145	4.37

Liver

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
105		73	11.8	41	15.19	209	13.71	137	12.74
106	11.7	74	10.3	42	13.08	210	13.69	138	12.7
107	12.13	75	12.02	43	11.09	211	13.14	140	13.08
108	10.96	76	14.51	44	12.22	212	11.78	141	11.81
109	13.12	77	10.57	45	13.77	213	10.77	142	12.35
110	10.9	78	12.97	227	14.03	214	9.47	143	11.14
111	10.29	79	12.19	47	11.9	215	11.75	144	10.99
112	11.96	80	15.08	48	11.57	216	12.54	145	11.65

Kidneys

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
105		73	2.34	41	2.58	209	2.49	137	2.42
106	2.15	74	2	42	1.95	210	2.62	138	2.24
107	1.81	75	2.27	43	2.04	211	2.72	140	2.35
108	2.16	76	2.21	44	2.27	212	2.48	141	2.47
109		77	1.66	45	2.17	213	1.97	142	2.45
110	1.87	78	2.1	227	2.67	214	1.73	143	2.1
111	2.27	79	2.3	47	2.43	215	2.4	144	1.98
112	1.86	80	2.73	48	2.23	216	2.21	145	2.53

Brain

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
105		73	1.56	41	1.95	209	1.93	137	1.99
106	1.67	74	1.6	42	1.76	210	2.24	138	1.8
107	1.62	75	1.95	43	1.81	211		140	1.98
108	1.7	76	1.62	44	1.05	212	2.03	141	1.92
109	1.63	77	1.75	45	1.75	213	1.72	142	2.04
110	1.98	78	1.65	227	1.59	214	1.97	143	2.02
111	2.34	79	2.2	47	1.83	215	2.09	144	1.9
112	2.2	80	1.77	48	1.94	216	1.96	145	2.12

Sex Organs

High Dose		*Mid Dose*		*Low Dose*		*Control*[a]		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
105		73	1.11	41	1.69	209	1.07	137	2.8
106	1.83	74	0.75	42	1.34	210	1.56	138	1.73
107	1.17	75	1.65	43	2.35	211	1.66	140	2.88
108	1.16	76	1.6	44	1.18	212	2.25	141	1.81
109	2.28	77	1.42	45	0.92	213	0.96	142	3.47
110	1.07	78	0.96	227	1.37	214	0.63	143	1.44
111	1.48	79	2.15	47	1.98	215	1.16	144	2.33
112	2.4	80	2.33	48	2.27	216	1.23	145	1.69

Spleen

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
105		73	0.62	41	1.12	209	0.78	137	0.71
106	0.78	74	0.81	42	0.72	210	0.82	138	0.82
107	0.75	75	0.85	43	0.56	211	1.03	140	0.94
108	0.42	76	0.44	44	0.6	212	0.92	141	0.68
109	0.74	77	0.42	45	0.39	213	0.81	142	0.86
110	0.94	78	0.55	227	0.52	214	0.55	143	0.8
111	1.22	79	1.05	47	0.74	215	0.17	144	0.85
112	0.8	80	0.89	48	1.01	216	0.89	145	0.84

GI Tract

High Dose	*Mid Dose*	*Low Dose*	*Control*	*Naïve*

Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
105		73	29.83	41	29.91	209	33.94	137	37.74
106	23.87	74	22.82	42	31.86	210	34.12	138	32.02
107	25.28	75	25.24	43	29.63	211	30.75	140	37.01
108	29.29	76	31.58	44	28.42	212	33.96	141	28.47
109	28.02	77	25.15	45	33.05	213	21.56	142	36.68
110	24.63	78	38	227	42.59	214	22.14	143	24.32
111	23.68	79	29	47	30	215	28.43	144	29.7
112	25.09	80	33.25	48	26.96	216	30.65	145	27.79

[a]Different from naïve ($p<0.05$)

[b]Different from control ($p<0.05$)

Table 19. Organ Weights, Measured 14 days after the Final Exposure

Heart

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
113	0.99	81	1.3	49	0.77	217	1.3	146	0.94
114	0.75	82	1.28	50	1.22	218	1.32	147	1.02
115	0.84	83	0.66	51	1.01	219	0.77	149	1.2
116	0.68	84	1.07	52	0.91	220	1.3	150	0.88
117	0.77	85	0.86	53	0.84	221	1.21	151	1.03

Thoracic (Heart lungs thymus)

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
118	5.29	86	3.97	54	4.63	222	4.96	152	4.26
119	3.33	87	3.69	55	3.42	223	3.06	225	3.65
120	4.11	88	4.33	56	3.42	224	3.9	226	4.24

Liver

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
113	12.52	81	11.06	49	11.02	217	15.4	146	12.79
114	9.33	82	14.48	50	12.111	218	14.67	147	12.95
115	12.74	83	11.12	51	14.37	219	10.54	149	13.11
116	12.25	84	14.56	52	9.21	220	14.69	150	11.72
117	9.83	85	10.82	53	11.4	221	13.72	151	13.23
118	12.61	86	11.64	54	11.6	222	16	152	12.48
119	11.24	87	11.41	55	12.95	223	9.87	225	12.32
120	11.61	88	12.62	56	11.45	224	12.01	226	12.17

Kidneys

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
113	2.54	81	2.05	49	1.8	217	1.32	146	2.13
114	1.74	82	2.55	50	2.53	218	2.17	147	2.12
115	2.27	83	1.88	51	2.55	219	2.21	149	2.81
116	1.87	84	2.18	52	1.87	220	1.94	150	2.19

117	2.12	85	2.15	53	2.48	221	2.79	151	2.51
118	1.8	86	1.65	54	1.9	222	2.5	152	2.08
119	2.1	87	1.74	55	2.15	223	1.24	225	1.89
120	1.93	88	2.16	56	1.36	224	1.66	226	2.15

Brain

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
113	1.69	81	1.61	49	1.79	217	1.9	146	1.28
114	1.53	82	1.6	50	1.94	218	1.79	147	1.74
115	1.74	83	1.58	51	1.97	219	1.75	149	1.6
116	1.79	84	1.68	52	1.63	220	1.77	150	1.79
117	1.66	85	1.83	53	1.5	221	1.49	151	1.93
118	1.78	86	1.53	54	1.71	222	1.84	152	
119	1.22	87	1.59	55	1.56	223	1.47	225	1.83
120	1.54	88	1.82	56	1.75	224	1.45	226	1.48

Sex Organs

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
113	3.48	81		49		217	3.32	146	3.82
114		82	4.23	50	3.15	218		147	
115	2.86	83		51	2.05	219	1.93	149	2.46
116		84		52		220		150	
117	2.37	85	2.53	53	1.96	221	3.3	151	2.8
118		86		54		222		152	
119		87		55		223		225	
120		88		56		224	4.6	226	

Spleen

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
113	0.55	81	0.62	49	0.59	217	0.54	146	0.37
114	0.31	82	0.42	50	0.49	218	0.42	147	0.4
115	0.51	83	0.58	51	0.53	219	0.47	149	0.49
116	0.58	84	0.84	52	0.63	220	0.7	150	0.52
117	0.45	85	0.61	53		221	0.5	151	
118	0.82	86	0.26	54	0.51	222	0.61	152	0.72
119	0.24	87	0.44	55	0.59	223	0.46	225	0.25
120	0.39	88	0.38	56	0.43	224	0.37	226	0.5

GI Tract

High Dose		*Mid Dose*		*Low Dose*		*Control*		*Naïve*	
Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)	Animal #	Weight (g)
113	30.15	81	31.82	49	22.18	217	36.41	146	34.44
114	22.22	82	32.82	50	32.44	218	37.37	147	31.72
115	28.31	83	27.27	51	36.4	219	22.86	149	30.66
116	27.18	84	35.13	52	18.91	220	41.26	150	26.69
117	20.49	85	29.31	53	24.57	221	33.53	151	36.26

118	28.57	86	29.46	54	30.83	222	40.5	152	26.9
119	26.56	87	32.66	55	30.52	223	22.75	225	24.56
120	22.43	88	30.9	56	28.39	224	28.69	226	33.14

Identifying Information

Table 20. Animal Identification Codes

Animal #s	Treatment
25- 32	Air—Jugular vein catheters
33-45, 47-56	Low Concentration—Intact
57-64	Low Concentration— Jugular vein catheters
65-88	Medium Concentration—Intact
89-96	Medium Concentration-- Jugular vein catheters
97-120	High Concentration—Intact
121-128	High Concentration— Jugular vein catheters
129-152	Naïve—Intact
153-160	Naïve—Jugular vein catheters
201- 224	Air—Intact
225-226	Naïve—Intact
227	Low Concentration—Intact

CBC with Differential

Table 21. 24 hr CBC with Differential

Animal number	**202**	**203**	**204**	**205**	**33**	**34**	**36**	**68**
WBC (x10^3/µl)	12.43	8.90	10.71	10.60	9.25	9.36	12.20	12.77
RBC (x10^6/µl)	7.35	7.10	6.94	7.55	7.42	7.06	7.39	7.56
HGB (g/dl)	13.8	14.2	14.2	15.0	14.6	14.4	14.8	14.7
HCT (%)	40.6	41.1	41.8	42.6	41.4	41.1	40.9	44.0
MCV (fL)	55.2	57.9	60.2	56.4	55.8	58.2	55.4	58.2
MCH (pg)	18.8	20.0	20.5	19.8	19.6	20.4	20.0	19.5
MCHC (g/dl)	34.1	34.6	34.0	35.1	35.2	35.1	36.1	33.4
CHCM (g/dl)	33.3	33.4	33.4	33.8	33.0	33.4	34.5	32.6
CH (pg)	18.4	19.3	20.0	19.0	18.4	19.4	19.1	19.0
RDW (%)	10.6	11.0	11.4	11.6	10.8	11.5	11.0	10.9
HD (g/dl)	2.37	2.41	2.67	2.26	2.24	2.32	2.51	2.28
PLT (x10^3/µl)	1411	948	898	1149	1215	1244	1013	1139
MPV (fL)	8.6	9.3	10.1	10.4	9.5	9.6	9.3	10.4
% NEUT	5.0	10.9	10.5	9.5	9.9	6.8	7.1	5.1
% LYMPH	93.4	85.8	86.5	87.4	87.9	90.6	90.9	92.4
% MONO	0.4	1.1	1.1	1.3	1.1	0.8	0.6	1.1
% EOS	0.6	1.6	1.0	1.0	0.6	1.2	0.8	0.7
% BASO	0.3	0.3	0.4	0.3	0.2	0.2	0.3	0.5
% LUC	0.3	0.5	0.5	0.5	0.3	0.3	0.3	0.3
#NEUT (x10^3/µl)	0.62	0.97	1.13	1.01	0.91	0.64	0.87	0.65

Animal number	202	203	204	205	33	34	36	68
#LYMPH (x10^3/µl)	11.61	7.63	9.26	9.26	8.13	8.48	11.09	11.79
#MONO (x10^3/µl)	0.05	0.10	0.12	0.14	0.10	0.08	0.07	0.13
#EOS (x10^3/µl)	0.08	0.14	0.11	0.11	0.06	0.12	0.10	0.09
#BASO (x10^3/µl)	0.04	0.02	0.05	0.03	0.02	0.02	0.04	0.06
#LUC (x10^3/µl)	0.04	0.04	0.05	0.05	0.02	0.02	0.04	0.03

Table 21. 24 hr CBC with Differential cont'd

Animal number	69	97	98	99	100	101	129	130
WBC (x10^3/µl)	5.80	8.43	6.86	14.98	13.15	13.70	8.12	6.80
RBC (x10^6/µl)	7.15	7.48	7.60	7.22	7.53	7.04	7.00	6.66
HGB (g/dl)	14.5	14.8	14.4	14.5	15.7	14.5	13.5	13.2
HCT (%)	40.9	43.8	41.7	41.4	43.5	42.5	40.1	39.2
MCV (fL)	57.1	58.5	54.8	57.3	57.7	60.8	57.2	58.8
MCH (pg)	20.3	19.8	19.0	20.1	20.9	20.7	19.3	19.9
MCHC (g/dl)	35.5	33.8	34.7	35.1	36.2	34.0	33.7	33.8
CHCM (g/dl)	33.4	32.0	33.2	33.1	34.1	33.1	32.3	32.9
CH (pg)	19.0	18.7	18.1	18.9	19.6	20.0	18.4	19.3
RDW (%)	11.0	11.2	11.9	11.6	10.5	11.2	11.0	11.4
HD (g/dl)	2.24	2.58	2.67	2.20	2.66	2.43	2.25	2.48
PLT (x10^3/µl)	157	893	912	899	824	1221	1027	1095
MPV (fL)	30.1	9.9	9.8	9.2	11.3	9.8	9.1	8.9
% NEUT	6.2	15.2	13.9	7.0	18.6	9.9	11.0	12.0
% LYMPH	91.5	81.8	82.8	90.0	78.1	87.5	85.5	85.5
% MONO	0.7	0.8	1.0	1.2	1.3	0.8	1.4	0.5
% EOS	0.8	1.5	1.5	0.8	0.8	1.0	1.5	1.7
% BASO	0.4	0.3	0.3	0.3	0.5	0.3	0.2	0.1
% LUC	0.4	0.3	0.5	0.7	0.7	0.5	0.4	0.2
#NEUT (x10^3/µl)	0.36	1.28	0.96	1.05	2.44	1.35	0.89	0.81
#LYMPH (x10^3/µl)	5.31	6.89	5.67	13.48	10.27	11.98	6.95	5.82
#MONO (x10^3/µl)	0.04	0.07	0.07	0.18	0.18	0.11	0.12	0.03
#EOS (x10^3/µl)	0.04	0.13	0.10	0.12	0.11	0.14	0.12	0.11
#BASO (x10^3/µl)	0.03	0.03	0.02	0.05	0.07	0.04	0.01	0.01
#LUC (x10^3/µl)	0.02	0.03	0.04	0.10	0.09	0.07	0.03	0.02

Table 21. 24 hr CBC with Differential cont'd

Animal number	131	132
WBC (x10^3/µl)	9.16	8.62
RBC (x10^6/µl)	6.97	6.72
HGB (g/dl)	13.3	13.8
HCT (%)	38.9	40.4
MCV (fL)	55.7	60.2
MCH (pg)	19.1	20.5
MCHC (g/dl)	34.2	34.0
CHCM (g/dl)	32.7	32.5
CH (pg)	18.2	19.5
RDW (%)	11.0	10.9

Animal number	131	132
HD (g/dl)	2.31	2.25
PLT (x10^3/µl)	936	899
MPV (fL)	9.7	10.8
% NEUT	15.0	8.0
% LYMPH	81.0	89.2
% MONO	1.5	0.9
% EOS	1.1	1.4
% BASO	0.2	0.2
% LUC	1.1	0.2
#NEUT (x10^3/µl)	1.37	0.69
#LYMPH (x10^3/µl)	7.42	7.68
#MONO (x10^3/µl)	0.14	0.08
#EOS (x10^3/µl)	0.10	0.12
#BASO (x10^3/µl)	0.02	0.02
#LUC (x10^3/µl)	0.10	0.02

Micro clots were present on the sample from animal 69; very few platelets, no platelet clumps, no large platelets were observed on slide review.

The samples for the following animals were clotted and unable to be analyzed: 201, 35, 37, 65, 66, 67, and 133.

Table 22. 7-Day CBC with Differential

Animal number	210	211	212	213	41	42	43	44
WBC (x10^3/µl)	9.47	9.98	13.20	11.26	10.23	9.04	9.80	5.43
RBC (x10^6/µl)	6.80	7.23	7.13	7.14	6.01	6.64	7.43	5.83
HGB (g/dl)	13.7	14.1	14.0	13.7	12.1	13.3	14.8	11.7
HCT (%)	38.7	40.1	39.1	38.0	33.9	39.1	40.8	32.5
MCV (fL)	56.6	55.5	54.8	53.3	56.5	58.8	54.9	55.7
MCH (pg)	20.2	19.5	19.6	19.1	20.1	20.0	19.9	20.1
MCHC (g/dl)	35.7	35.1	35.8	35.9	35.6	34.0	36.2	36.1
CHCM (g/dl)	35.1	34.0	35.0	36.1	34.3	33.7	35.6	35.1
CH (pg)	19.8	18.8	19.1	19.2	19.3	19.7	19.5	19.5
RDW (%)	11.5	11.4	11.1	12.3	13.0	13.0	10.6	10.6
HD (g/dl)	2.78	2.40	2.64	2.73	2.63	2.40	2.60	2.58
PLT (x10^3/µl)	792	678	754	1137	834	781	968	727
MPV (fL)	10.6	8.9	10.0	9.1	9.7	8.9	11.9	12.1
% NEUT	9.7	3.9	10.7	12.0	5.7	15.1	12.8	6.0
% LYMPH	87.1	93.7	86.9	85.7	91.4	79.7	84.3	90.1
% MONO	0.7	0.5	0.5	1.0	0.8	0.9	0.7	0.8
% EOS	1.8	1.4	0.9	0.9	1.2	3.8	1.5	2.2
% BASO	0.3	0.2	0.6	0.3	0.5	0.4	0.3	0.7
% LUC	0.4	0.4	0.4	0.2	0.4	0.2	0.3	0.2
#NEUT (x10^3/µl)	0.92	0.39	1.41	1.35	0.58	1.36	1.26	0.33
#LYMPH (x10^3/µl)	8.24	9.34	11.48	9.64	9.36	7.20	8.26	4.89
#MONO (x10^3/µl)	0.06	0.05	0.06	0.11	0.08	0.08	0.07	0.04
#EOS (x10^3/µl)	0.17	0.14	0.12	0.10	0.12	0.34	0.15	0.12
#BASO (x10^3/µl)	0.03	0.02	0.07	0.03	0.06	0.04	0.03	0.04
#LUC (x10^3/µl)	0.04	0.04	0.05	0.02	0.04	0.02	0.03	0.01

Table 22. 7-Day CBC with Differential (cont'd)

Animal number	45	73	74	75	76	77	106	107
WBC ($x10^3$/µl)	6.91	12.54	5.93	8.64	9.19	11.69	21.40	7.91
RBC ($x10^6$/µl)	6.49	6.81	7.62	7.36	7.16	6.95	7.40	6.67
HGB (g/dl)	12.4	14.0	14.5	15.1	13.6	13.7	14.5	13.8
HCT (%)	34.7	40.4	40.9	42.0	38.1	38.5	40.6	37.6
MCV (fL)	53.4	59.4	53.7	57.1	53.2	55.4	54.9	56.5
MCH (pg)	19.1	20.6	19.0	20.5	19.0	19.7	19.6	20.7
MCHC (g/dl)	35.9	34.6	35.4	35.9	35.7	35.5	35.7	36.7
CHCM (g/dl)	36.1	34.1	34.9	35.5	35.5	35.0	35.4	36.8
CH (pg)	19.2	20.2	18.7	20.2	18.9	19.4	19.4	20.7
RDW (%)	11.7	11.4	11.4	11.3	10.9	11.1	10.9	11.2
HD (g/dl)	2.72	2.45	2.33	2.72	2.39	2.60	2.62	2.75
PLT ($x10^3$/µl)	668	745	690	762	660	943	621	498
MPV (fL)	9.7	9.8	9.7	9.4	9.2	8.6	9.8	10.0
% NEUT	23.5	10.2	19.7	16.4	11.1	18.3	10.6	18.9
% LYMPH	71.2	87.0	76.5	79.0	85.2	78.5	86.8	76.5
% MONO	1.5	0.6	0.5	1.4	0.9	1.0	0.5	0.7
% EOS	3.0	1.7	3.0	2.6	2.3	1.8	1.3	3.3
% BASO	0.4	0.3	0.2	0.4	0.2	0.2	0.5	0.3
% LUC	0.4	0.3	0.1	0.2	0.2	0.2	0.4	0.2
#NEUT ($x10^3$/µl)	1.63	1.27	1.17	1.41	1.02	2.14	2.27	1.50
#LYMPH ($x10^3$/µl)	4.92	10.90	4.54	6.83	7.84	9.18	18.57	6.05
#MONO ($x10^3$/µl)	0.11	0.07	0.03	0.12	0.08	0.12	0.10	0.05
#EOS ($x10^3$/µl)	0.21	0.22	0.18	0.23	0.21	0.22	0.28	0.26
#BASO ($x10^3$/µl)	0.03	0.04	0.01	0.03	0.02	0.02	0.10	0.03
#LUC ($x10^3$/µl)	0.03	0.03	0.01	0.02	0.02	0.02	0.09	0.02

Table 22. 7-Day CBC with Differential (cont'd)

Animal number	108	109	137	138	140	141	142
WBC ($x10^3$/µl)	15.85	8.13	10.75	13.28	11.47	8.57	16.67
RBC ($x10^6$/µl)	7.21	7.13	6.51	6.53	7.09	6.00	7.53
HGB (g/dl)	14.5	14.5	13.1	13.1	14.3	12.3	14.9
HCT (%)	41.1	40.6	36.9	36.9	39.9	33.8	42.3
MCV (fL)	57.0	56.9	56.6	56.5	56.2	56.4	56.2
MCH (pg)	20.1	20.3	20.1	20.0	20.2	20.5	19.8
MCHC (g/dl)	35.2	35.7	35.6	35.4	35.9	36.3	35.3
CHCM (g/dl)	34.9	35.6	34.5	34.3	35.8	34.7	34.8
CH (pg)	19.8	20.2	19.5	19.3	20.1	19.5	19.5
RDW (%)	11.1	11.2	10.5	10.9	11.0	11.1	10.8
HD (g/dl)	2.40	2.50	2.66	2.54	2.48	2.77	2.50
PLT ($x10^3$/µl)	720	661	892	778	547	963	627
MPV (fL)	9.3	8.8	9.4	9.8	8.3	10.4	9.2
% NEUT	8.7	16.8	4.5	8.1	10.4	4.5	7.8
% LYMPH	87.9	80.1	92.3	89.3	85.8	91.1	89.1
% MONO	0.5	1.2	1.2	0.5	1.0	0.7	0.7
% EOS	2.3	1.3	0.6	0.9	2.2	1.7	1.5
% BASO	0.3	0.4	0.7	0.6	0.4	1.0	0.7
% LUC	0.3	0.2	0.7	0.6	0.3	1.0	0.3

Animal number	108	109	137	138	140	141	142
#NEUT (x10^3/µl)	1.38	1.36	0.48	1.08	1.19	0.38	1.29
#LYMPH (x10^3/µl)	13.93	6.51	9.93	11.86	9.84	7.80	14.86
#MONO (x10^3/µl)	0.08	0.10	0.13	0.07	0.11	0.06	0.11
#EOS (x10^3/µl)	0.37	0.10	0.06	0.11	0.26	0.15	0.24
#BASO (x10^3/µl)	0.05	0.04	0.08	0.08	0.04	0.08	0.11
#LUC (x10^3/µl)	0.05	0.02	0.07	0.08	0.03	0.09	0.05

The samples for the following animals were clotted and unable to be analyzed: 105 and 209.

Table 23. 14-Day CBC with Differential

Animal number	49	50	51	52	53	54	81	82
WBC (x10^3/µl)	7.10	11.29	7.64	7.66	8.13	13.26	14.14	6.43
RBC (x10^6/µl)	7.51	7.84	7.30	8.02	7.12	6.78	7.18	6.40
HGB (g/dl)	14.6	14.6	14.2	14.9	13.8	13.9	13.9	12.9
HCT (%)	43.4	43.0	41.5	44.6	41.1	40.5	42.0	37.5
MCV (fL)	57.8	54.9	56.9	55.7	57.7	59.7	58.5	58.6
MCH (pg)	19.4	18.6	19.5	18.5	19.4	20.5	19.4	20.1
MCHC (g/dl)	33.6	33.9	34.3	33.3	33.7	34.4	33.2	34.4
CHCM (g/dl)	33.3	32.9	33.0	31.7	33.0	33.2	31.1	32.7
CH (pg)	19.1	18.0	18.6	17.6	19.0	19.7	18.1	19.1
RDW (%)	12.2	11.8	12.5	12.2	11.9	12.9	11.7	13.1
HD (g/dl)	2.69	2.83	2.83	2.56	2.72	2.89	2.73	2.62
PLT (x10^3/µl)	947	801	929	794	681	794	911	757
MPV (fL)	8.4	8.3	8.7	8.9	9.5	9.7	9.3	8.5
% NEUT	8.2	19.9	17.6	8.8	10.2	6.6	11.7	9.9
% LYMPH	87.9	76.9	79.2	88.4	86.9	91.4	85.3	86.9
% MONO	1.1	0.8	1.0	0.8	1.1	0.4	1.2	1.1
% EOS	2.2	1.5	1.5	1.6	1.4	0.9	1.0	1.8
% BASO	0.2	0.3	0.1	0.1	0.2	0.3	0.3	0.1
% LUC	0.3	0.5	0.5	0.2	0.2	0.4	0.5	0.2
#NEUT (x10^3/µl)	0.59	2.25	1.35	0.67	0.83	0.88	1.66	0.64
#LYMPH (x10^3/µl)	6.24	8.68	6.05	6.77	7.07	12.12	12.06	5.59
#MONO (x10^3/µl)	0.08	0.10	0.08	0.06	0.09	0.06	0.17	0.07
#EOS (x10^3/µl)	0.16	0.17	0.11	0.12	0.11	0.11	0.14	0.11
#BASO (x10^3/µl)	0.02	0.03	0.01	0.01	0.02	0.03	0.04	0.01
#LUC (x10^3/µl)	0.02	0.06	0.04	0.02	0.01	0.05	0.08	0.01

Table 23. 14-Day CBC with Differential (cont'd)

Animal number	83	84	85	113	114	115	116	117
WBC (x10^3/µl)	11.11	11.29	8.47	7.14	4.71	5.49	7.32	4.86
RBC (x10^6/µl)	7.39	7.47	6.87	6.49	6.39	7.61	7.02	7.09
HGB (g/dl)	14.3	14.2	13.9	13.3	12.8	15.2	13.5	14.0
HCT (%)	41.7	41.7	39.3	39.0	37.3	45.5	39.6	42.3
MCV (fL)	56.5	55.9	57.3	60.1	58.3	59.8	56.4	59.6
MCH (pg)	19.4	19.0	20.2	20.5	20.0	20.0	19.2	19.7
MCHC (g/dl)	34.4	34.0	35.3	34.1	34.3	33.4	34.0	33.0
CHCM (g/dl)	32.2	32.9	33.3	32.4	32.3	31.9	32.1	31.9

Animal number	83	84	85	113	114	115	116	117
CH (pg)	18.1	18.3	19.0	19.4	18.8	19.0	18.0	18.9
RDW (%)	11.6	13.0	12.1	12.2	11.8	12.2	12.2	12.7
HD (g/dl)	2.42	2.93	2.59	2.66	2.46	2.37	2.63	2.53
PLT ($x10^3$/µl)	800	874	1054	784	980	1155	807	974
MPV (fL)	8.7	8.2	8.5	8.5	9.5	9.2	9.0	8.4
% NEUT	8.2	8.8	7.1	9.9	8.9	15.3	8.1	14.2
% LYMPH	89.9	88.9	91.0	88.2	87.7	81.1	88.7	82.8
% MONO	0.8	0.8	0.6	0.7	0.9	1.1	1.1	1.2
% EOS	0.6	1.2	0.8	0.9	2.0	2.1	1.6	1.1
% BASO	0.2	0.2	0.3	0.2	0.1	0.1	0.1	0.2
% LUC	0.3	0.1	0.4	0.2	0.4	0.2	0.5	0.5
#NEUT ($x10^3$/µl)	0.91	1.00	0.60	0.71	0.42	0.84	0.59	0.69
#LYMPH ($x10^3$/µl)	9.99	10.04	7.70	6.29	4.13	4.45	6.49	4.02
#MONO ($x10^3$/µl)	0.09	0.09	0.05	0.05	0.04	0.06	0.08	0.06
#EOS ($x10^3$/µl)	0.07	0.13	0.07	0.06	0.10	0.12	0.11	0.05
#BASO ($x10^3$/µl)	0.02	0.03	0.02	0.01	0.00	0.01	0.01	0.01
#LUC ($x10^3$/µl)	0.03	0.01	0.03	0.01	0.02	0.01	0.03	0.02

Table 23. 14-Day CBC with Differential (cont'd)

Animal number	146	147	149	150	151	152	217	219
WBC ($x10^3$/µl)	12.22	12.94	7.40	11.79	5.96	7.63	7.31	6.29
RBC ($x10^6$/µl)	6.83	7.20	7.17	7.20	7.24	7.33	6.94	7.53
HGB (g/dl)	13.8	13.7	14.0	14.2	14.3	14.3	13.4	13.8
HCT (%)	42.1	39.8	42.1	42.1	42.0	43.4	40.5	43.0
MCV (fL)	61.7	55.3	58.7	58.5	58.1	59.1	58.4	57.1
MCH (pg)	20.2	19.0	19.6	19.7	19.8	19.5	19.4	18.3
MCHC (g/dl)	32.8	34.3	33.3	33.8	34.1	33.0	33.2	32.0
CHCM (g/dl)	31.7	32.6	32.5	31.9	32.3	31.7	32.1	31.6
CH (pg)	19.5	18.0	19.0	18.6	18.7	18.6	18.7	18.0
RDW (%)	11.7	11.6	11.9	11.7	11.7	1.20	12.1	12.6
HD (g/dl)	2.64	2.65	2.67	2.56	2.66	2.68	2.52	2.36
PLT ($x10^3$/µl)	917	845	986	969	820	878	911	874
MPV (fL)	8.1	8.8	7.7	8.0	8.0	8.4	9.5	8.6
% NEUT	15.4	6.0	12.5	5.9	10.2	12.0	5.6	10.5
% LYMPH	82.0	91.8	84.7	92.1	87.5	84.5	91.6	86.7
% MONO	0.8	0.8	0.9	0.6	0.8	0.9	0.6	1.0
% EOS	1.1	0.9	1.2	0.9	1.2	2.0	1.9	1.4
% BASO	0.2	0.2	0.2	0.3	0.1	0.1	0.2	0.1
% LUC	0.5	0.3	0.5	0.3	0.2	0.4	0.3	0.3
#NEUT ($x10^3$/µl)	1.88	0.78	0.93	0.69	0.61	0.92	0.41	0.66
#LYMPH ($x10^3$/µl)	10.03	11.88	6.27	10.85	5.22	6.45	6.69	5.45
#MONO ($x10^3$/µl)	0.10	0.10	0.07	0.07	0.05	0.07	0.04	0.06
#EOS ($x10^3$/µl)	0.13	0.12	0.09	0.10	0.07	0.15	0.14	0.09
#BASO ($x10^3$/µl)	0.02	0.03	0.02	0.03	0.01	0.01	0.01	0.01
#LUC ($x10^3$/µl)	0.06	0.03	0.03	0.04	0.01	0.03	0.02	0.02

Table 23. 14-Day CBC with Differential (cont'd)

Animal number	220	221
WBC ($x10^3$/µl)	8.42	8.90
RBC ($x10^6$/µl)	7.12	6.69
HGB (g/dl)	14.2	12.8
HCT (%)	41.7	38.3
MCV (fL)	58.6	57.2
MCH (pg)	19.9	19.2
MCHC (g/dl)	34.0	33.5
CHCM (g/dl)	32.3	32.5
CH (pg)	18.8	18.5
RDW (%)	12.5	12.6
HD (g/dl)	2.73	2.70
PLT ($x10^3$/µl)	762	987
MPV (fL)	8.8	8.2
% NEUT	20.9	8.3
% LYMPH	76.1	89.3
% MONO	1.4	0.7
% EOS	1.1	0.9
% BASO	0.1	0.3
% LUC	0.4	0.1
#NEUT ($x10^3$/µl)	1.76	0.74
#LYMPH ($x10^3$/µl)	6.41	7.95
#MONO ($x10^3$/µl)	0.12	0.07
#EOS ($x10^3$/µl)	0.09	0.08
#BASO ($x10^3$/µl)	0.01	0.02
#LUC ($x10^3$/µl)	0.03	0.04

The sample for animal 215 was clotted and unable to be analyzed.

Clinical Chemistry

Table 24. Clinical Chemistry Blood Data Prior to and During the Exposure Period

		TBIL (mg/dl)	AST (U/l)	ALT (U/l)	ALP (U/l)	LDH (U/l)	CREA (mg/dl)	BUN (mg/dl)	TP (g/dl)
25 PRE	air	1.4	64	35	76	161	0.5	15	5.9
26 PRE	air	0.6	57	37	140	98	0.5	18	7.1
28 PRE	air	1.3	55	27	170	152	0.5	18	6.3
29 PRE	air	1	66	35	149	150	0.5	17	5.8
30 PRE	air	1.4	50	29	135	129	0.6	18	6.4
31 PRE	air	0.6	64	38	125	120	0.5	18	6.6
57 PRE	low	0.8	47	18	120	98	0.5	16	5.9
58 PRE	low	0.6	85	59	95	118	0.5	20	7.7
59 PRE	low	1	69	34	128	157	0.5	14	6.2
60 PRE	low	0.3	58	45	80	114	0.5	16	6.9
61 PRE	low	1	57	39	135	129	0.5	18	6
62 PRE	low	1.2	58	39	181	143	0.5	17	5.9

		TBIL (mg/dl)	AST (U/l)	ALT (U/l)	ALP (U/l)	LDH (U/l)	CREA (mg/dl)	BUN (mg/dl)	TP (g/dl)
89 PRE	mid	0.7	50	36	167	113	0.4	17	6.2
90 PRE	mid	0.3	54	35	127	100	0.5	17	6.3
91 PRE	mid	0.3	44	24	72	94	0.4	12	6.1
92 PRE	mid	0.5	80	55	120	167	0.4	15	6.6
93 PRE	mid	0.8	59	37	161	164	0.6	17	6.1
94 PRE	mid	0.4	60	32	147	163	0.5	14	6.2
121 PRE	high	0.7	49	29	89	136	0.4	18	5.9
122 PRE	high	1.3	43	34	120	127	0.5	16	7.1
123 PRE	high	0.4	54	33	124	137	0.5	13	6.4
124 PRE	high	0.3	49	22	65	128	0.5	17	6.5
125 PRE	high	0.3	63	42	141	105	0.5	16	6.6
126 PRE	high	0.4	53	33	137	105	0.6	19	6.4
127 PRE	high	0.3	60	39	93	110	0.6	21	6.5
128 PRE	high	0.5	64	37	137	181	0.5	14	6.3
153 PRE	naïve	0.5	74	40	152	147	0.6	21	6.4
154 PRE	naïve	0.8	54	36	129	209	0.4	19	6.8
155 PRE	naïve	0.9	63	30	150	182	0.5	20	6.6
156 PRE	naïve	0.4	53	35	189	112	0.5	19	6.1
157 PRE	naïve	0.6	56	28	85	195	0.6	16	5.3
160 PRE	naïve	0.3	83	43	111	174	0.6	18	6.6
26 MID	air	0.7	59	39	134	209	0.4	20	6.4
28 MID	air	1.3	55	30	173	167	0.5	18	6.5
29 MID	air	1.2	63	31	164	119	0.6	18	5.9
31 MID	air	0.7	78	32	107	135	0.6	21	6.3
57 MID	low	0.4	76	29	142	109	0.5	17	6.8
59 MID	low	1	78	34	132	97	0.5	21	6.5
60 MID	low	0.6	46	30	91	107	0.5	19	7.2
62 MID	low	0.9	70	36	163	198	0.5	24	6.8
89 MID	mid	2.1	45	25	111	270	0.6	21	6
90 MID	mid	1.4	52	34	128	93	0.5	20	6
91 MID	mid	0.8	52	35	97	59	0.5	18	6
92 MID	mid	1.5	79	51	142	146	0.6	20	7
93 MID	mid	0.6	66	38	173	113	0.4	18	6.1
94 MID	mid	1.3	50	27	130	59	0.5	19	5.8
121 MID	high	0.6	51	28	120	74	0.4	22	6.4
122 MID	high	1.8	49	32	168	130	0.4	20	7.8
123 MID	high	0.6	52	21	115	91	0.5	18	6.1
125 MID	high	0.7	57	25	131	115	0.6	18	6.5
126 MID	high	0.7	60	32	150	115	0.6	24	6.9
127 MID	high	0.6	66	26	99	110	0.6	19	6.7
128 MID	high	2.1	69	30	106	254	0.6	20	6.3
153 MID	naïve	2.5	78	39	176	229	0.5	22	7.1
154 MID	naïve	1.6	61	42	134	160	0.5	19	7.1
155 MID	naïve	0.6	77	44	169	259	0.5	17	6.6
157 MID	naïve	0.7	57	30	125	110	0.4	18	6.2
25 TS	air	0.4	68	37	138	164	0.4	17	6.3
26 TS	air	1.2	68	39	113	253	0.4	15	7.2
28 TS	air	0.8	69	31	139	222	0.5	14	7.4

		TBIL (mg/dl)	AST (U/l)	ALT (U/l)	ALP (U/l)	LDH (U/l)	CREA (mg/dl)	BUN (mg/dl)	TP (g/dl)
29 TS	air	0.5	56	27	177	172	0.4	13	5.6
30 TS	air	1.1	51	26	90	230	0.4	15	7.4
31 TS	air	0.4	64	38	117	145	0.5	14	6.6
57 TS	low	0.4	79	41	106	155	0.4	15	7
59 TS	low	0.4	52	27	97	202	0.4	15	6.1
60 TS	low	0.4	48	32	70	121	0.4	13	6.8
61 TS	low	0.6	57	33	145	174	0.4	18	6.4
62 TS	low	0.3	72	33	114	163	0.4	17	5.6
89 TS	mid	0.6	64	31	126	244	0.5	19	6.4
90 TS	mid	0.3	85	47	122	157	0.4	16	6.4
91 TS	mid	0.6	55	23	161	202	0.5	21	6.5
92 TS	mid	0	39	34	101	96	0.4	15	6.2
93 TS	mid	0.3	57	31	133	103	0.4	15	5.9
94 TS	mid	0.3	60	34	113	215	0.5	17	6.1
121 TS	high	0.3	58	35	82	72	0.5	19	6.6
122 TS	high	1.7	49	33	101	211	0.5	21	7.2
123 TS	high	0.4	67	46	119	127	0.5	16	7.6
124 TS	high	1.3	47	24	73	161	0.5	16	6.4
125 TS	high	0.4	49	32	105	130	0.5	15	6.1
126 TS	high	1.9	61	37	97	233	0.4	21	6.8
127 TS	high	2.1	67	43	110	188	0.5	24	6.9
128 TS	high	0.4	50	27	82	149	0.4	13	6.4
153 TS	naïve	0.9	63	34	105	241	0.4	16	6.1
154 TS	naïve	4.2	70	41	101	360	0.4	23	7.4
155 TS	naïve	0.5	50	27	83	236	0.4	17	5.9
156 TS	naïve	0.7	65	42	163	202	0.5	21	6.7
157 TS	naïve	0.5	51	26	75	167	0.4	14	5.5
160 TS	naïve	0.9	72	56	99	129	0.4	14	7.1

Table 25. Clinical Chemistry Blood Data 24 hrs after the Final Exposure

Group/ Animal #	TBIL (mg/dl)	AST (U/l)	ALT (U/l)	ALP (U/l)	PHOS (mg/dl)	LDH (U/l)	CREA (mg/dl)	BUN (mg/dl)	TP (g/dl)
C201	2.2	120	57	98	8.6	704	0.4	20	6.8
C202	0.6	49	32	114	7	214	0.5	21	6
C203	0.5	79	35	73	6.4	968	0.5	20	6.4
C204	1.3	79	32	107	7.8	900	0.5	18	6.5
C205	0.9	99	38	115	7.1	1091[a]	0.4	17	6.1
C206	3.5	122	50	137	8.8	1519[a]	0.4	23	7.1
C207	4.3	83	47	199	9.5	833	0.4	18	7.6
C208	0.6	60	36	100	7.9	287	0.4	14	7.5
H100	0.8	51	35	88	8.8	303	0.5	20	6.5
H101	1.3	77	38	144	8.6	628	0.4	18	6.4
H102	0.6	87	35	153	8.5	874	0.3	16	6.3
H103	0.9	83	30	190	8.6	1147[a]	0.3	19	6
H104	0.8	72	30	110	8	904	0.4	16	6.8
H97	0.6	75	33	107	10	676	0.5	18	5.6

Group/ Animal #	TBIL (mg/dl)	AST (U/l)	ALT (U/l)	ALP (U/l)	PHOS (mg/dl)	LDH (U/l)	CREA (mg/dl)	BUN (mg/dl)	TP (g/dl)
H98	0.7	68	35	126	8.2	652	0.5	24	5.9
H99	1	64	40	116	8.7	519	0.5	25	6.2
L33	0.5	49	28	142	7.4	234	0.4	22	5.7
L34	0.4	49	32	155	8.1	126	0.4	21	5.8
L35	0.6	50	38	96	8.1	189	0.4	22	6
L36	0.7	95	34	111	7.7	1738[a]	0.3	20	5.8
L37	0.5	62	25	93	8.7	573	0.5	19	5.5
L39	2.3	106	33	96	9.2	1366[a]	0.4	19	6.9
L40	4.6	90	40	124	9.8	1153[a]	0.3	21	7.2
M65	3.4	150	49	100	11.8	2028[a]	0.5	22	7.1
M66	0.8	82	38	139	7.4	976	0.4	18	6.3
M67	0	16	36	117	8.1	509	0.4	18	6.3
M68	1.6	51	38	118	9.1	297	0.5	19	6
M69	3.2	101	33	116	9.8	1493[a]	0.4	20	6.8
M70	1.7	93	37	122	8.5	1134[a]	0.4	19	6.4
M72	1.8	106	36	148	10.6	1354[a]	0.4	16	6.4
N129	0.8	69	37	131	8.8	671	0.4	21	5.9
N130	1.1	77	38	121	7.7	816	0.5	20	5.7
N131	1.6	65	39	145	7.3	581	0.4	20	6.3
N132	0.8	59	39	104	7.9	412	0.5	18	5.9
N133	0.9	90	52	183	8.6	553	0.5	22	6.1
N134	1.2	99	41	154	6.9	533	0.3	15	5.8
N135	0.3	49	34	112	7.4	80	0.3	17	5.6
N136	2.7	72	51	113	9	466	0.6	22	7.3

[a]Bloody sample; excluded from statistical analysis.

Table 26. Clinical Chemistry Blood Data 7 days after the Final Exposure

Group/ Animal #	TBIL (mg/dl)	AST (U/l)	ALT (U/l)	ALP (U/l)	PHOS (mg/dl)	LDH (U/l)	CREA (mg/dl)	BUN (mg/dl)	TP (g/dl)
C209	5.1	114	50	88	10	958	0.5	25	7.4
C210	1.1	49	42	152	6.4	84	0.4	22	6.2
C212	2.7	64	42	105	6.6	220	0.4	26	6.5
C213	0.8	98	43	97	4.5	383	0.4	18	6
C214	0.3	47	25	72	7.5	107	0.4	15	5.4
C215	0.6	50	32	134	7.3	104	0.4	19	6
C216	0.3	55	47	107	8.7	243	0.4	15	5.9
H105	0.4	55	37	125	8.2	152	0.5	19	5.8
H106	0.3	43	26	83	7.1	148	0.4	15	6.3
H107	0.5	52	26	101	7.2	202	0.4	18	6.2
H108	0.3	54	44	130	7.4	104	0.4	23	6.2
H109	0.4	52	40	153	7.6	118	0.5	18	6.3
H110	0.3	53	42	70	7.4	181	0.4	14	5.5
H111	0.4	43	25	87	6.8	116	0.5	19	5.9
H112	0.4	53	38	100	7.2	156	0.3	17	5.8
L41	1.2	63	35	103	7.2	181	0.3	18	5.7
L42	0.6	75	37	113	7.4	314	0.5	25	5.4
L43	0.7	71	51	180	6.6	294	0.5	29	6.1
L45	1.4	117	58	137	6	204	0.3	19	6.5

Group/ Animal #	TBIL (mg/dl)	AST (U/l)	ALT (U/l)	ALP (U/l)	PHOS (mg/dl)	LDH (U/l)	CREA (mg/dl)	BUN (mg/dl)	TP (g/dl)
L46	0.7	49	33	143	6.4	97	0.3	20	5.9
L47	0.4	50	36	190	7.3	95	0.4	21	6.2
L48	0.3	42	34	122	7.6	81	0.4	18	5.8
M73	0.4	46	39	197	6.5	110	0.4	21	5.9
M74	0.6	48	31	95	6.6	116	0.4	20	6.7
M75	0.4	53	36	122	7	126	0.4	20	6
M76	2.6	78	37	80	7.6	458	0.3	20	6.7
M77	0.4	44	36	119	6.4	89	0.4	24	6.1
M78	1.3	44	31	104	7.5	106	0.3	23	6.4
M79	0.1	17	18	86	4.7	101	0.4	17	5.6
M80	0.6	38	41	96	7.1	72	0.4	22	6.3
N137	2.1	76	35	226	7.2	544	0.3	23	6.1
N138	3.3	97	61	126	8	835	0.4	20	6.2
N140	7.7	81	45	78	9.2	1189[a]	0.4	21	6.7
N141	2.7	153	53	170	8.8	1423[a]	0.3	21	5.9
N142	0.8	51	41	114	5.9	64	0.4	21	5.5
N143	0.6	58	41	95	6.9	124	0.5	16	5.7
N144	1	41	25	116	6.3	87	0.4	20	5.6
N145	0.4	53	39	101	7.8	123	0.5	18	5.8

[a]Bloody sample; excluded from statistical analysis.

Table 27. Clinical Chemistry Blood Data 14 days after the Final Exposure

Group/ Animal #	TBIL (mg/dl)	AST (U/l)	ALT (U/l)	ALP (U/l)	PHOS (mg/dl)	LDH (U/l)	CREA (mg/dl)	BUN (mg/dl)	TP (g/dl)
C217	2	46	37	119	7.4	112	0.4	23	6.4
C218	3.3	151	99	135	7.7	374	0.5	27	7.6
C219	0.8	47	48	113	5.5	81	0.5	18	6.5
C220	0.7	52	47	133	7.1	101	0.5	23	6
C221	1.2	79	56	113	7.4	112	0.4	22	6.5
C222	0.5	36	37	96	7.7	57	0.4	20	6.3
C223	0.2	42	42	205	8.1	82	0.4	15	6.1
C224	1.4	44	34	96	7.3	111	0.5	20	6
H113	0.4	46	33	128	6.4	64	0.4	24	6.1
H114	0.7	66	27	141	6	92	0.5	19	5.6
H115	0.7	7	41	95	7.6	242	0.5	22	6.9
H116	0.3	66	30	99	6.8	148	0.5	20	6.5
H117	3	72	43	99	8.8	405	0.5	18	6.4
H118	0.4	38	32	105	8.3	77	0.4	15	6.3
H119	0.2	43	47	93	8.2	93	0.5	18	6.3
H120	0.5	102	63	93	8.8	277	0.5	17	6.8
L49	0.3	45	33	121	5.9	108	0.4	18	6.3
L50	1	97	49	181	6.5	596	0.4	21	6
L51	0.9	104	54	87	6.6	319	0.3	24	7.1
L52	0.3	50	34	96	6.3	127	0.5	15	6.3
L53	0.7	50	39	151	6.2	112	0.5	18	6.1
L54	0.4	63	40	90	6.6	126	0.5	21	6.1
L55	0.2	44	47	115	8.5	108	0.5	21	7.1
L56	0.7	37	31	99	6.7	77	0.3	18	6.5

Group/ Animal #	TBIL (mg/dl)	AST (U/l)	ALT (U/l)	ALP (U/l)	PHOS (mg/dl)	LDH (U/l)	CREA (mg/dl)	BUN (mg/dl)	TP (g/dl)
M81	0.6	67	26	141	5.9	74	0.5	23	6
M82	5.1	60	48	85	8.1	288	0.3	22	8.5
M83	1.8	72	46	92	6.3	99	0.4	22	6
M84	0.3	71	46	85	5.9	132	0.4	20	5.6
M85	0.3	47	38	112	6	100	0.4	15	5.7
M86	0.3	44	36	103	7.2	64	0.4	18	6.3
M87	0.5	51	33	146	8.4	280	0.5	21	5.6
M88	0.5	51	42	93	7.8	108	0.5	17	6.8
N146	1.9	51	40	110	7.5	172	0.4	23	6.2
N147	0.5	108	66	123	6.7	189	0.5	22	5.8
N149	0.8	56	47	164	6.4	135	0.5	17	6.4
N150	0.5	43	37	120	7	81	0.4	19	6.3
N151	1	51	44	189	6.3	74	0.5	22	6
N152	0.4	52	40	152	6.5	190	0.6	19	6.5
N225	0.3	39	30	66	7.3	97	0.5	17	6.2
N226	0.3	49	32	142	8.1	73	0.5	20	5.8

Lung Lavage Cell Count and Differential

Table 28. Lung Lavage Cell Data 24 hrs after the Final Exposure

	129 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	99	1	0	
	Q3	99	1	0	
	Q4	100	0	0	
	%	99.5	0.5	0	
		0.995	0.005	0	
Total Cells	345960	344230.2	1729.8	0	
	130 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	98	2	0	
	Q3	99	1	0	
	Q4	99	1	0	
	%	98.75	1.25	0	
		0.9875	0.0125	0	
Total Cells	484800	478740	6060	0	
	131 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	100	0	0	
	Q3	100	0	0	
	Q4	100	0	0	
	%	100	0	0	

		1	0	0	
Total Cells	473400	473400	0	0	
	132 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	100	0	0	
	Q3	100	0	0	
	Q4	100	0	0	
	%	100	0	0	
		1	0	0	
Total Cells	456240	456240	0	0	
	133 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	100	0	0	
	Q3	99	1	0	
	Q4	97	3	0	
	%	99	1	0	
		0.99	0.01	0	
Total Cells	257880	255301.2	2578.8	0	
	201 C Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	99	1	0	0
	Q2	99	1	0	0
	Q3	100	0	0	0
	Q4	96	2	1	1
	%	98.5	1	0.25	0.25
		0.985	0.01	0.0025	0.0025
Total Cells	330000	325050	3300	825	825
	202 C Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	98	2	0	
	Q3	98	2	0	
	Q4	98	2	0	
	%	98.25	1.75	0	
		0.9825	0.0175	0	
Total Cells	270480	265746.6	4733.4	0	
	203 C Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	96	4	0	
	Q2	96	4	0	
	Q3	95	4	1	
	Q4	97	3	0	
	%	96	3.75	0.25	
		0.96	0.0375	0.0025	
Total Cells	207000	198720	7762.5	517.5	
	204 C Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	96	3	1	0

	Q2	96	4	0	0
	Q3	93	6	0	1
	Q4	98	2	0	0
	%	95.75	3.75	0.25	0.25
		0.9575	0.0375	0.0025	0.0025
Total Cells	458640	439147.8	17199	1146.6	1146.6
	205 C Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	98	1	1	0
	Q2	98	1	0	1
	Q3	98	1	1	0
	Q4	99	0	1	0
	%	98.25	0.75	0.75	0.25
		0.9825	0.0075	0.0075	0.0025
Total Cells	249000	244642.5	1867.5	1867.5	622.5
	33 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	98	2	0	
	Q2	96	3	1	
	Q3	99	1	0	
	Q4	98	2	0	
	%	97.75	2	0.25	
		0.9775	0.02	0.0025	
Total Cells	310320	303337.8	6206.4	775.8	
	34 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	98	2	0	
	Q2	96	4	0	
	Q3	98	2	0	
	Q4	96	4	0	
	%	97	3	0	
		0.97	0.03	0	
Total Cells	433200	420204	12996	0	
	35 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	99	1	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	99.25	0.75	0	
		0.9925	0.0075	0	
Total Cells	314400	312042	2358	0	
	36 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	100	0	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	99.5	0.5	0	
		0.995	0.005	0	

Total Cells	606480	603447.6	3032.4	0	
	37 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	96	3	1	
	Q2	98	2	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.25	1.5	0.25	
		0.9825	0.015	0.0025	
Total Cells	415920	408641.4	6238.8	1039.8	
	65 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	94	4	2	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.25	1.25	0.5	
		0.9825	0.0125	0.005	
Total Cells	356280	350045.1	4453.5	1781.4	
	66 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	97	2	1	
	Q2	97	1	2	
	Q3	95	2	3	
	Q4	94	4	2	
	%	95.75	2.25	2	
		0.9575	0.0225	0.02	
Total Cells	323160	309425.7	7271.1	6463.2	
	67 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	93	0	7	
	Q2	94	0	6	
	Q3	96	0	4	
	Q4	94	0	6	
	%	94.25	0	5.75	
		0.9425	0	0.0575	
Total Cells	305160	287613.3	0	17546.7	
	68 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	97	3	0	
	Q2	97	3	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.25	1.75	0	
		0.9825	0.0175	0	
Total Cells	438960	431278.2	7681.8	0	
	69 M Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	97	2	1	0
	Q2	100	0	0	0

	Q3	97	1	2	0
	Q4	98	1	0	1
	%	98	1	0.75	0.25
		0.98	0.01	0.0075	0.0025
Total Cells	237840	233083.2	2378.4	1783.8	594.6
	97 H Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	98	2	0	
	Q2	98	2	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.75	1.25	0	
		0.9875	0.0125	0	
Total Cells	307320	303478.5	3841.5	0	
	98 H Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	99	0	0	1
	Q2	98	2	1	0
	Q3	98	1	1	0
	Q4	96	3	1	0
	%	97.75	1.5	0.75	0.25
		0.9775	0.015	0.0075	0.0025
Total Cells	228840	223691.1	3432.6	1716.3	572.1
	99 H Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	0	1	
	Q2	99	0	1	
	Q3	100	0	0	
	Q4	96	1	3	
	%	98.5	0.25	1.25	
		0.985	0.0025	0.0125	
Total Cells	320160	315357.6	800.4	4002	
	100 H Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	97	0	3	0
	Q2	98	0	2	0
	Q3	98	0	2	0
	Q4	94	1	5	0
	%	96.75	0.25	3	0
		0.9675	0.0025	0.03	0
Total Cells	231240	223724.7	578.1	6937.2	0
	101 H Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	95	2	1	2
	Q2	92	6	0	2
	Q3	93	7	0	0
	Q4	93	6	1	0
	%	93.25	5.25	0.5	1
		0.9325	0.0525	0.005	0.01

Total Cells	512640	478036.8	26913.6	2563.2	5126.4

Table 29. Lung Lavage Cell Data 7 days after the Final Exposure

	137 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	99	1	0	
	Q3	99	1	0	
	Q4	100	0	0	
	%	99.5	0.5	0	
		0.995	0.005	0	
Total Cells	90000	89550	450	0	
	138 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	98	2	0	
	Q3	99	1	0	
	Q4	99	1	0	
	%	98.75	1.25	0	
		0.9875	0.0125	0	
Total Cells	327500	323406.25	4093.75	0	
	140 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	100	0	0	
	Q3	100	0	0	
	Q4	100	0	0	
	%	100	0	0	
		1	0	0	
Total Cells	262500	262500	0	0	
	141 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	100	0	0	
	Q3	100	0	0	
	Q4	100	0	0	
	%	100	0	0	
		1	0	0	
Total Cells	352500	352500	0	0	
	142 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	100	0	0	
	Q3	99	1	0	
	Q4	97	3	0	
	%	99	1	0	
		0.99	0.01	0	
Total Cells	142500	141075	1425	0	

	209 C Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	99	1	0	0
	Q2	99	1	0	0
	Q3	100	0	0	0
	Q4	96	2	1	1
	%	98.5	1	0.25	0.25
		0.985	0.01	0.0025	0.0025
Total Cells	417500	411237.5	4175	1043.75	1043.75
	210 C Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	98	2	0	
	Q3	98	2	0	
	Q4	98	2	0	
	%	98.25	1.75	0	
		0.9825	0.0175	0	
Total Cells	427500	420018.75	7481.25	0	
	211 C Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	96	4	0	
	Q2	96	4	0	
	Q3	95	4	1	
	Q4	97	3	0	
	%	96	3.75	0.25	
		0.96	0.0375	0.0025	
Total Cells	290000	278400	10875	725	
	212 C Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	96	3	1	0
	Q2	96	4	0	0
	Q3	93	6	0	1
	Q4	98	2	0	0
	%	95.75	3.75	0.25	0.25
		0.9575	0.0375	0.0025	0.0025
Total Cells	725000	694187.5	27187.5	1812.5	1812.5
	213 C Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	98	1	1	0
	Q2	98	1	0	1
	Q3	98	1	1	0
	Q4	99	0	1	0
	%	98.25	0.75	0.75	0.25
		0.9825	0.0075	0.0075	0.0025
Total Cells	830000	815475	6225	6225	2075
	41 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	98	2	0	
	Q2	96	3	1	
	Q3	99	1	0	

	Q4	98	2	0	
	%	97.75	2	0.25	
		0.9775	0.02	0.0025	
Total Cells	227500	222381.25	4550	568.75	
	42 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	98	2	0	
	Q2	96	4	0	
	Q3	98	2	0	
	Q4	96	4	0	
	%	97	3	0	
		0.97	0.03	0	
Total Cells	302500	293425	9075	0	
	43 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	99	1	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	99.25	0.75	0	
		0.9925	0.0075	0	
Total Cells	340000	337450	2550	0	
	44 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	100	0	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	99.5	0.5	0	
		0.995	0.005	0	
Total Cells	522500	519887.5	2612.5	0	
	45 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	96	3	1	
	Q2	98	2	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.25	1.5	0.25	
		0.9825	0.015	0.0025	
Total Cells	700000	687750	10500	1750	
	73 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	94	4	2	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.25	1.25	0.5	
		0.9825	0.0125	0.005	
Total Cells	582500	572306.25	7281.25	2912.5	

	74 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	97	2	1	
	Q2	97	1	2	
	Q3	95	2	3	
	Q4	94	4	2	
	%	95.75	2.25	2	
		0.9575	0.0225	0.02	
Total Cells	870000	833025	19575	17400	
	75 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	93	0	7	
	Q2	94	0	6	
	Q3	96	0	4	
	Q4	94	0	6	
	%	94.25	0	5.75	
		0.9425	0	0.0575	
Total Cells	240000	226200	0	13800	
	76 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	97	3	0	
	Q2	97	3	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.25	1.75	0	
		0.9825	0.0175	0	
Total Cells	1165000	1144612.5	20387.5	0	
	77 M Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	97	2	1	0
	Q2	100	0	0	0
	Q3	97	1	2	0
	Q4	98	1	0	1
	%	98	1	0.75	0.25
		0.98	0.01	0.0075	0.0025
Total Cells	450000	441000	4500	3375	1125
	105 H Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	98	2	0	
	Q2	98	2	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.75	1.25	0	
		0.9875	0.0125	0	
Total Cells	530000	523375	6625	0	
	106 H Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	99	0	0	1
	Q2	98	2	1	0
	Q3	98	1	1	0

	Q4	96	3	1	0
	%	97.75	1.5	0.75	0.25
		0.9775	0.015	0.0075	0.0025
Total Cells	660000	645150	9900	4950	1650
	107 H Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	0	1	
	Q2	99	0	1	
	Q3	100	0	0	
	Q4	96	1	3	
	%	98.5	0.25	1.25	
		0.985	0.0025	0.0125	
Total Cells	1090000	1073650	2725	13625	
	108 H Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	97	0	3	0
	Q2	98	0	2	0
	Q3	98	0	2	0
	Q4	94	1	5	0
	%	96.75	0.25	3	0
		0.9675	0.0025	0.03	0
Total Cells	1165000	1127137.5	2912.5	34950	0
	109 H Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	95	2	1	2
	Q2	92	6	0	2
	Q3	93	7	0	0
	Q4	93	6	1	0
	%	93.25	5.25	0.5	1
		0.9325	0.0525	0.005	0.01
Total Cells	610000	568825	32025	3050	6100

Table 30. Lung Lavage Cell Data 14 days after the Final Exposure

	146 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	99	1	0	
	Q3	99	1	0	
	Q4	100	0	0	
	%	99.5	0.5	0	
		0.995	0.005	0	
Total Cells	185900	184970.5	929.5	0	
	147 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	98	2	0	
	Q3	99	1	0	
	Q4	99	1	0	
	%	98.75	1.25	0	

		0.9875	0.0125	0	
Total Cells	200000	197500	2500	0	
	149 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	100	0	0	
	Q3	100	0	0	
	Q4	100	0	0	
	%	100	0	0	
		1	0	0	
Total Cells	283000	283000	0	0	
	150 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	100	0	0	
	Q3	100	0	0	
	Q4	100	0	0	
	%	100	0	0	
		1	0	0	
Total Cells	233000	233000	0	0	
	151 N Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	100	0	0	
	Q3	99	1	0	
	Q4	97	3	0	
	%	99	1	0	
		0.99	0.01	0	
Total Cells	155500	153945	1555	0	
	217 C Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	99	1	0	0
	Q2	99	1	0	0
	Q3	100	0	0	0
	Q4	96	2	1	1
	%	98.5	1	0.25	0.25
		0.985	0.01	0.0025	0.0025
Total Cells	180000	177300	1800	450	450
	218 C Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	98	2	0	
	Q3	98	2	0	
	Q4	98	2	0	
	%	98.25	1.75	0	
		0.9825	0.0175	0	
Total Cells	167200	164274	2926	0	
	219 C Lung 1	Macrophages	PMN	Lymphocytes	

	Q1	96	4	0	
	Q2	96	4	0	
	Q3	95	4	1	
	Q4	97	3	0	
	%	96	3.75	0.25	
		0.96	0.0375	0.0025	
Total Cells	248200	238272	9307.5	620.5	
	220 C Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	96	3	1	0
	Q2	96	4	0	0
	Q3	93	6	0	1
	Q4	98	2	0	0
	%	95.75	3.75	0.25	0.25
		0.9575	0.0375	0.0025	0.0025
Total Cells	175200	167754	6570	438	438
	221 C Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	98	1	1	0
	Q2	98	1	0	1
	Q3	98	1	1	0
	Q4	99	0	1	0
	%	98.25	0.75	0.75	0.25
		0.9825	0.0075	0.0075	0.0025
Total Cells	200000	196500	1500	1500	500
	49 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	98	2	0	
	Q2	96	3	1	
	Q3	99	1	0	
	Q4	98	2	0	
	%	97.75	2	0.25	
		0.9775	0.02	0.0025	
Total Cells	249700	244081.75	4994	624.25	
	50 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	98	2	0	
	Q2	96	4	0	
	Q3	98	2	0	
	Q4	96	4	0	
	%	97	3	0	
		0.97	0.03	0	
Total Cells	619300	600721	18579	0	
	51 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	99	1	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	99.25	0.75	0	

		0.9925	0.0075	0	
Total Cells	225000	223312.5	1687.5	0	
	52 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	1	0	
	Q2	100	0	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	99.5	0.5	0	
		0.995	0.005	0	
Total Cells	299000	297505	1495	0	
	53 L Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	96	3	1	
	Q2	98	2	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.25	1.5	0.25	
		0.9825	0.015	0.0025	
Total Cells	178000	174885	2670	445	
	81 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	100	0	0	
	Q2	94	4	2	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.25	1.25	0.5	
		0.9825	0.0125	0.005	
Total Cells	117700	115640.25	1471.25	588.5	
	82 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	97	2	1	
	Q2	97	1	2	
	Q3	95	2	3	
	Q4	94	4	2	
	%	95.75	2.25	2	
		0.9575	0.0225	0.02	
Total Cells	228000	218310	5130	4560	
	83 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	93	0	7	
	Q2	94	0	6	
	Q3	96	0	4	
	Q4	94	0	6	
	%	94.25	0	5.75	
		0.9425	0	0.0575	
Total Cells	209000	196982.5	0	12017.5	
	84 M Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	97	3	0	

	Q2	97	3	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.25	1.75	0	
		0.9825	0.0175	0	
Total Cells	338000	332085	5915	0	
	85 M Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	97	2	1	0
	Q2	100	0	0	0
	Q3	97	1	2	0
	Q4	98	1	0	1
	%	98	1	0.75	0.25
		0.98	0.01	0.0075	0.0025
Total Cells	200800	196784	2008	1506	502
	113 H Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	98	2	0	
	Q2	98	2	0	
	Q3	100	0	0	
	Q4	99	1	0	
	%	98.75	1.25	0	
		0.9875	0.0125	0	
Total Cells	221200	218435	2765	0	
	114 H Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	99	0	0	1
	Q2	98	2	1	0
	Q3	98	1	1	0
	Q4	96	3	1	0
	%	97.75	1.5	0.75	0.25
		0.9775	0.015	0.0075	0.0025
Total Cells	213200	208403	3198	1599	533
	115 H Lung 1	Macrophages	PMN	Lymphocytes	
	Q1	99	0	1	
	Q2	99	0	1	
	Q3	100	0	0	
	Q4	96	1	3	
	%	98.5	0.25	1.25	
		0.985	0.0025	0.0125	
Total Cells	240400	236794	601	3005	
	116 H Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	97	0	3	0
	Q2	98	0	2	0
	Q3	98	0	2	0
	Q4	94	1	5	0
	%	96.75	0.25	3	0
		0.9675	0.0025	0.03	0

Total Cells	206100	199401.75	515.25	6183	0
	117 H Lung 1	Macrophages	PMN	Lymphocytes	Eosinophils
	Q1	95	2	1	2
	Q2	92	6	0	2
	Q3	93	7	0	0
	Q4	93	6	1	0
	%	93.25	5.25	0.5	1
		0.9325	0.0525	0.005	0.01
Total Cells	233800	218018.5	12274.5	1169	2338

Lung Lavage Biomarkers

Table 31. Total Protein in Lung Lavage Fluid (µg/ml)

Rat #/dose	24 hrs after final exposure	Rat #/dose	7 days after final exposure	Rat #/dose	14 days after final exposure
129 N	82.22	137 N	94.09367	146 N	46.68933
130 N	91.11067	138 N	90.62567	147 N	107.948
131 N	90.607	140 N	75.50767	149 N	71.058
132 N	87.92233	141 N	96.521	150 N	43.73
133 N	82.10433	142 N	76.22033	151 N	56.86033
201 C	115.4733	209 C	131.366	217 C	85.18433
202 C	86.616	210 C	140.7023	218 C	90.377
203 C	93.84167	211 C	100.2113	219 C	68.403
204 C	87.67067	212 C	77.518	220 C	73.203
205 C	78.44333	213 C	106.5573	221 C	118.692
33 L	77.43867	41 L	128.6047	49 L	182.06
34 L	84.55467	42 L	172.4297	50 L	89.052
35 L	89.85367	43 L	120.1693	51 L	95.05367
36 L	93.54433	44 L	124.591	52 L	34.36333
37 L	90.44467	45 L	127.444	53 L	97.368
65 M	88.63367	73 M	108.6753	81 M	131.3627
66 M	75.42533	74 M	106.7973	82 M	90.7635
67 M	193.4477	75 M	64.926	83 M	91.96067
68 M	106.8997	76 M	173.7883	84 M	235.485
69 M	107.5663	77 M	101.225	85 M	161.8347
97 H	109.018	105 H	122.9053	113 H	65.44233
98 H	93.15833	106 H	76.33067	114 H	56.57267
99 H	96.36633	107 H	no data	115 H	78.952
100 H	135.222	108 H	130.169	116 H	127.1635
101 H	100.0663	109 H	85.201	117 H	85.201

Table 32. LDH Levels in Lung Lavage Fluid (ng/ml)

Rat dose group	24 hrs after final exposure	Rat #/dose	7 days after final exposure	Rat #/dose	14 days after final exposure
N	271.2	137 N	386.039	146 N	549.927
N	463.32	138 N	277.939	147 N	174.692
N	281.832	140 N	452.5347	149 N	188.3757
N	468.852	141 N	383.8417	150 N	187.4787
N	205.776	142 N	305.5677	151 N	169.7597
A	218.52	209 C	488.907	217 C	289.0485
A	296.292	210 C	456.4947	218 C	253.691
A	361.836	211 C	469.463	219 C	148.8943
A	144.636	212 C	332.171	220 C	261.4213
A	339.732	213 C	833.24	221 C	196.5925
L	267.372	41 L	693.908	49 L	154.4543
L	620.88	42 L	751.582	50 L	179.4013
L	346.38	43 L	866.3543	51 L	269.0743
L	385.596	44 L	759.2103	52 L	181.343
L	216.552	45 L	1419.436	53 L	203.2407
M	339.72	73 M	392.334	81 M	248.1033
M	182.976	74 M	446.5453	82 M	220.421
M	904.272	75 M	282.5357	83 M	186.1317
M	304.572	76 M	431.733	84 M	304.264
M	314.472	77 M	557.6737	85 M	184.31
H	531.828	105 H	777.259	113 H	202.6303
H	143.016	106 H	517.9143	114 H	349.8327
H	370.896	107 H	No data	115 H	228.773
H	401.124	108 H	424.4763	116 H	329.5453
H	513.816	109 H	555.5217	117 H	191.6557

Table 33. Beta Glucuronidase Levels in Lung Lavage Fluid (µg/ml)

Rat #/dose	24 hrs after final exposure	Rat #/dose	7 days after final exposure	Rat #/dose	14 days after final exposure
129 N	57.11967	137 N	81.46567	146 N	81.16167
130 N	50.81233	138 N	87.45833	147 N	76.828
131 N	55.47833	140 N	104.8757	149 N	75.58533
132 N	123.2303	141 N	97.58833	150 N	68.99867
133 N	62.29933	142 N	84.86033	151 N	89.58033
201 C	57.06433	209 C	85.507	217 C	87.06567
202 C	60.77667	210 C	82.94133	218 C	81.95633
203 C	52.81133	211 C	88.77367	219 C	76.43367
204 C	63.37267	212 C	87.34933	220 C	74.207
205 C	62.46	213 C	129.918	221 C	78.26867

Rat #/dose	24 hrs after final exposure	Rat #/dose	7 days after final exposure	Rat #/dose	14 days after final exposure
33 L	76.97667	41 L	90.208	49 L	68.63633
34 L	111.172	42 L	74.077	50 L	75.05233
35 L	50.371	43 L	69.69833	51 L	80.67667
36 L	49.82633	44 L	90.54033	52 L	81.445
37 L	73.46367	45 L	121.6077	53 L	74.90667
65 M	53.481	73 M	109.4807	81 M	59.539
66 M	74.35333	74 M	79.714	82 M	75.26333
67 M	209.2503	75 M	129.4943	83 M	73.916
68 M	47.77167	76 M	81.45033	84 M	64.07233
69 M	87.229	77 M	85.33967	85 M	73.51967
97 H	63.31367	105 H	124.8437	113 H	70.459
98 H	83.72833	106 H	135.1273	114 H	76.765
99 H	76.917	107 H	no data	115 H	56.148
100 H	90.50867	108 H	103.7047	116 H	72.58
101 H	46.412	109 H	90.81267	117 H	60.78567

Nasal Lavage Biomarkers

Table 34. Total Protein in Nasal Lavage Fluid (µg/ml)

Rat #/dose	24 hrs after final exposure	Rat #/dose	7 days after final exposure	Rat #/dose	14 days after final exposure
129 N	72.92467	137 N	89.16533	146 N	113.5113
130 N	38.45867	138 N	119.6537	147 N	87.68213
131 N	63.08933	140 N	134.459	149 N	92.329
132 N	no data	141 N	236.0333	150 N	43.44033
133 N	75.56533	142 N	86.32967	151 N	77.978
201 C	53.27733	209 C	no data	217 C	140.7703
202 C	77.306	210 C	142.0353	218 C	118.6473
203 C	no data	211 C	64.718	219 C	77.135
204 C	106.694	212 C	154.806	220 C	109.1673
205 C	52.46667	213 C	132.2803	221 C	87.05933
33 L	63.245	41 L	93.33233	49 L	113.8027
34 L	75.09033	42 L	96.44133	50 L	111.918
35 L	217.5767	43 L	97.467	51 L	123.2107
36 L	106.8297	44 L	222.9033	52 L	107.328
37 L	104.1913	45 L	139.836	53 L	88.49933
65 M	195.4057	73 M	182.9333	81 M	98.22533
66 M	70.25867	74 M	101.4987	82 M	103.7947
67 M	85.94733	75 M	117.2663	83 M	117.052
68 M	75.94867	76 M	240.992	84 M	110.389

Rat #/dose	24 hrs after final exposure	Rat #/dose	7 days after final exposure	Rat #/dose	14 days after final exposure
69 M	81.80833	77 M	167.765	85 M	81.509
97 H	78.277	105 H	224.1117	113 H	103.816
98 H	130.5073	106 H	151.0853	114 H	104.1067
99 H	31.74033	107 H	185.764	115 H	74.09833
100 H	119.0637	108 H	209.9853	116 H	95.81067
101 H	142.646	109 H	310.622	117 H	85.201

Table 35. LDH Levels in Nasal Lavage Fluid (ng/ml)

Rat #/dose	24 hrs after final exposure	Rat #/dose	7 days after final exposure	Rat #/dose	14 days after final exposure
N	135.688	Unknown/N	476.112	146 N	208.401
N	449.148	Unknown/N	523.32	147 N	352.75
N	114.688	Unknown/N	158.97	149 N	194.048
N	397.894	Unknown/N	94.122	150 N	106.8707
N	no data	Unknown/N	no data	151 N	275.764
C	289.058	209 C	no data	217 C	476.6585
C	240.828	210 C	293.403	218 C	454.3477
C	449.722	211 C	470.239	219 C	325.683
C	240.926	212 C	497.9977	220 C	158.3163
C	no data	213 C	313.1127	221 C	208.008
L	258.622	41 L	881.8307	49 L	764.436
L	546.994	42 L	483.1777	50 L	437.4333
L	503.412	43 L	250.0033	51 L	208.399
L	235.27	44 L	624.89	52 L	112.5173
L	78.624	45 L	469.113	53 L	723.076
M	257.362	73 M	599.9073	81 M	366.6423
M	58.548	74 M	219.2827	82 M	575.1877
M	437.192	75 M	406.6623	83 M	288.0167
M	246.974	76 M	766.1177	84 M	413.4953
M	349.846	77 M	205.4133	85 M	529.635
H	527.45	105 H	708.8737	113 H	277.5175
H	215.95	106 H	646.9257	114 H	338.759
H	517.804	107 H	512.508	115 H	340.775
H	155.008	108 H	377.1433	116 H	314.8905
H	no data	109 H	619.9	117 H	373.5547

Table 36. Beta Glucuronidase Levels in Nasal Lavage Fluid (µg/ml)

Rat #/dose	24 hrs after final exposure	Rat #/dose	7 days after final exposure	Rat #/dose	14 days after final exposure
129 N	70.597	137 N	129.416	146 N	79.342
130 N	60.623	138 N	100.562	147 N	91.857
131 N	68.406	140 N	104.202	149 N	86.466
132 N	no data	141 N	146.873	150 N	88.397
133 N	113.653	142 N	80.172	151 N	76.108
201 C	85.115	209 C	no data	217 C	84.536
202 C	82.867	210 C	76.371	218 C	86.706
203 C	no data	211 C	86.870	219 C	85.715
204 C	79.339	212 C	77.250	220 C	87.766
205 C	92.738	213 C	128.890	221 C	87.690
33 L	101.405	41 L	79.735	49 L	84.176
34 L	85.345	42 L	96.442	50 L	90.407
35 L	96.097	43 L	88.717	51 L	86.258
36 L	80.978	44 L	105.983	52 L	88.690
37 L	91.813	45 L	97.262	53 L	63.518
65 M	95.679	73 M	78.145	81 M	90.435
66 M	88.760	74 M	79.755	82 M	80.134
67 M	87.480	75 M	90.100	83 M	84.528
68 M	93.293	76 M	86.352	84 M	77.869
69 M	105.195	77 M	88.782	85 M	81.444
97 H	98.774	105 H	81.787	113 H	78.879
98 H	76.083	106 H	79.363	114 H	73.108
99 H	78.572	107 H	97.192	115 H	71.947
100 H	76.643	108 H	77.915	116 H	76.044
101 H	88.765	109 H	92.278	117 H	78.360

Pathology Summary Report

Systemic Metabolic Response In Rats (*Rattus norvegicus*)
Exposed To Jet A Biphasic Atmospheres

Protocol Number: 0086
Date: 8 March 2006

Study Director: Erin Wilfong, PhD
Study Pathologist: Randall Rietcheck, DVM, DACVP

NARRATIVE PATHOLOGY REPORT for Accession Nos. 050350, 050352–050462 and 050503–050542

History:
Female rats were exposed to Jet A vapor/aerosol or air 7 days/week, 1.5 hours/day for 14 days. Urine and blood samples were obtained at various time points before, during, and after exposure. Animals were sacrificed by 70% CO_2 exposure 24 hrs after the last Jet A or air exposure and metabolite profiles in the blood and urine were analyzed. A separate set of animals were sacrificed by injecting sodium pentobarbital 24 hrs, 7 days, and 14 days after the last Jet A exposure for histopathologic examination.

Gross observations:
Not available.

Microscopic findings:
The histopathologic diagnoses are listed on individual animal Pathology Reports identified by the assigned, unique Accession Number.

Comment:
Of interest was the presence of mineralization occurring within the cytoplasm of renal tubular epithelial cells within the majority of female rats evaluated histologically. Mineralization was restricted to a focally extensive region near the corticomedullary junction and in most instances was not associated with any inflammatory or other tissue reaction. Many tubular lumens within this region also contained mineralized concretions (microlithiasis). This change is found more commonly in female rats and is considered an incidental finding usually associated with the level of hydration.

Most tissues evaluated were considered to be within normal limits. Other lesions diagnosed in the various tissues during the evaluation were often considered incidental findings that were judged to have been clinically insignificant. These types of changes or lesions can often be attributed to individual species characteristics, gender, age, or dietary influence. Background pathology, or those lesions frequently found in laboratory rats and considered within normal limits, were not coded as an official diagnosis. Incidental lesions noted during evaluation are discussed below.

In several rats, infiltrates composed of small numbers of eosinophils were present around small caliber arterioles within lung sections. Although the cause is unknown, they are considered an incidental finding.

Small foci of chronic inflammation were present within the kidneys of several rats. Occasionally, these foci were associated with stromal collapse and fibrosis that resulted in a capsular depression and tubular changes. In other animals, the inflammation was primarily lymphocytic. In all instances, however, the areas of inflammation appeared to be of little clinical significance and unrelated to the study.

One rat (accession number 050364; animal number 91; 24 hr medium dose group) had a focally extensive area of inflammation composed of neutrophils and eosinophils affecting a single lung lobe. Granulation tissue was present in the overlying pleural surface. The cause for this lesion was not evident in the sections examined.

A focally extensive area of centrilobular necrosis was present in the liver of one animal. This type of lesion, and smaller lesions composed of subacute inflammation in other study rats, are commonly found multifocally and presumed to be due to a focus of ischemia or incidental bacteria in the enterohepatic circulation.

Lymphocytic inflammation that was occasionally associated with acinar atrophy was present in the pancreas of several animals. The cause was not clear, but in all cases was focal and appeared to be clinically insignificant.

The lining of few thyroid follicles in two rats displayed squamous metaplasia, filling the follicles with keratin debris. The change may represent a remnant of a developmental ultimobranchial body.

There was no evidence of any infectious, toxic, developmental, or neoplastic change occurring in any of the tissue sections evaluated.

Randall L. Rietcheck, DVM, Diplomate ACVP
LTC, Veterinary Corps, US Army
Chief, AFRL/HEPB/Pathology

APPENDIX B

Supporting Documentation for Phase 2 Toxicity Study

Exposure Characterization

Table 37. Chamber Concentrations (mg/m^3)

	Low Chamber					Medium Chamber				
Day			***Chamber***	***Aerosol***	***Total***			***Chamber***	***Aerosol***	***Total***
#	***mmad*[a]**	***σ_g***	***mg/m^3***	***mg/m^3***	***mg/m^3***	***mmad***	***σ_g***	***mg/m^3***	***mg/m^3***	***mg/m^3***
1			453	11.72	464.72			620	38.34	658.34
1	2.05	2.35	453	17.30	470.30	2.25	2.32	650	63.61	713.61
2			509	27.74	536.74			745	101.92	846.92
2	2.02	2.38	528	32.90	560.90	2.26	2.34	768	103.40	871.40
3			490	65.38	555.38			780	154.74	934.74
3	1.78	2.60	500	25.26	525.26	2.21	2.31	783	116.48	899.48
4			495	24.40	519.40			712	91.34	803.34
4	2.04	2.59	533	32.48	565.48	2.20	2.34	745	102.46	847.46
5			507	27.83	534.83			654	81.92	735.92
5	2.42	2.67	538	37.07	575.07	2.28	2.41	736	96.06	832.06
6			514	26.42	540.42			761	105.21	866.21
6	1.79	2.22	538	36.96	574.96	2.27	2.35	760	108.22	868.22
7			530	26.26	556.26			822	126.45	948.45
7	2.48	2.81	540	28.28	568.28	2.16	2.30	850	110.18	960.18
8			530	21.49	551.49			822	136.53	958.53
8	2.12	2.58	520	27.47	547.47	2.20	2.34	829	115.61	944.61
9			530	31.19	561.19			830	117.66	947.66
9	2.13	2.54	558	37.19	595.19	2.03	2.29	839	109.43	948.43
10			537	0.09	537.09			833	109.60	942.60
10	1.98	2.51	557	26.61	583.61	2.17	2.28	818	56.87	874.88
11			542	19.92	561.92			820	143.72	963.72
11	0.22	8.27	558	11.48	569.48	1.91	2.08	816	121.65	937.65
12			506	163.57	669.57			512	1.19	513.19
12	2.08	2.56	523	28.07	551.07	2.09	2.36	765	117.04	882.04
13			423	3.50	426.50			718	130.85	848.85
13	2.37	3.21	421	10.39	431.39	2.20	2.23	829	120.03	949.03
14			507	23.09	530.09			798	123.42	921.42
14	2.03	2.48	512	34.18843	546.19	2.34	2.51	808	104.67	912.67
Average	**1.96**	**2.98**	**512.57**	**30.65**	**543.22**	**2.18**	**2.32**	**765.11**	**103.88**	**868.99**
Std.Deviation	**0.54**	**1.54**	**36.49**	**28.82**	**48.85**	**0.11**	**0.09**	**78.28**	**31.97**	**104.77**
Precision	**0.28**	**0.52**	**0.07**	**0.94**	**0.09**	**0.05**	**0.04**	**0.10**	**0.31**	**0.12**

[a]MMAD in µm

Table 37. Chamber Concentrations (mg/m3) (cont'd)

	High Chamber				
Day			***Chamber***	***Aerosol***	***Total***
#	***mmad***	***σ_g***	***mg/m^3***	***mg/m^3***	***mg/m^3***
1			1448	347.39	1795.39
1	2.75	2.38	1560	348.54	1908.54

High Chamber					
Day			***Chamber***	***Aerosol***	***Total***
#	***mmad***	σ_g	mg/m^3	mg/m^3	mg/m^3
2			1550	355.52	1905.52
2	2.71	2.42	1585	308.19	1893.19
3			1525	380.39	1905.39
3	2.63	2.40	1529	380.97	1909.97
4			1557	311.77	1868.77
4	2.59	2.41	1650	474.90	2124.90
5			1548	367.94	1915.94
5	2.69	2.40	1648	362.33	2010.33
6			1588	337.68	1925.68
6	2.70	2.19	1650	435.27	2085.27
7			1600	406.26	2006.26
7	2.41	2.39	1694	397.32	2091.32
8			1625	333.06	1958.06
8	2.74	2.47	1654	389.29	2043.29
9			1526	284.98	1810.98
9	2.72	2.23	1624	432.94	2056.94
10			1592	266.45	1858.45
10	2.79	2.10	1658	243.00	1901.00
11			1608	371.49	1979.49
11	2.83	2.08	1753	387.61	2140.61
12			1614	511.65	2125.65
12	2.70	2.41	1755	527.28	2282.28
13			1448	347.39	1795.39
13	2.76	2.51	1644	440.71	2084.71
14			1579	377.78	1956.78
14	2.49	2.37	1662	426.52	2088.52
Average	**2.68**	**2.34**	**1602.64**	**376.95**	**1979.59**
Std. Deviation	**0.12**	**0.13**	**74.23**	**66.49**	**119.25**
Precision	**0.04**	**0.06**	**0.05**	**0.18**	**0.06**

Identifying Information

Table 38. Animal Identification Codes

Strain	Animal #s	Treatment
F344	1-8	Air
	9-16	Low Concentration
	17-24	Medium Concentration
	25-32	High Concentration
	33-40	Air
	41-48	Low Concentration
	49-56	Medium Concentration
	57-64	High Concentration
	65-80	Naïve

Strain	Animal #s	Treatment
Sprague-Dawley	81-88	Air
	89-96	Low Concentration
	97-104	Medium Concentration
	105-112	High Concentration
	113-120	Air
	121-128	Low Concentration
	129-136	Medium Concentration
	137-144	High Concentration
	145-160	Naïve

Individual Animal Body Weights

Table 39. Body Weights of Naïve Rats

Animal	8/29/06	9/5/06	9/11/06	9/13/06	9/15/06	9/18/06 Expo. day 0	9/20/06	9/22/06	9/25/06	9/27/06	9/29/06	10/2/06 Expo. day 14
65	102.1	124.8	132.8	134.2	134	139.9	138.8	139	144.2	147.9	146.6	149.6
66	98.9	120.2	135	136.6	136.4	134.3	136.9	137.7	139.7	143.3	147.6	148.2
67	105.2	130.6	131	143.5	140	148.3	146.8	148.5	154.3	155.8	160.7	161.5
68	105.8	125.3	134.6	138.7	138.2	145.8	145.2	146.5	152.6	151.9	156.2	156
69	114.1	126.5	132.1	140.1	134.1	143.1	142.9	147.9	154.8	157.7	157.1	162.2
70	117.4	138.4	145.1	148.3	145.4	150.6	148.3	149.6	153.7	154.2	155.8	159
71	112.2	134.7	140.1	142.7	140.9	148.5	147.8	151.1	156.1	159.7	161.8	166.2
72	107.2	123.7	134.5	132.7	137.4	138.5	139.4	139.7	144.9	148.9	152.8	155.6
73	103.7	127.2	130	131.7	133.4	138.2	135.7	137.8	141.6	144.3	145.7	151.6
74	105.9	129.6	135.4	139	135.1	138.3	138	139.4	142	145.5	148.2	149.6
75	109.4	126.1	131.4	141.2	132.7	136.9	140.8	142.5	147.3	150.2	151.3	153.2
76	107.2	130	142.8	142.2	143.2	139.6	147.5	148.8	150.9	154.3	154.4	157.3
77	113.5	130.3	139.2	142	142.6	147.1	147.2	148.6	154.2	156.2	160.3	161.3
78	109.8	126.4	133.9	136.6	136.7	145.6	140	143.6	150.8	154.9	157.7	156.4
79	117.5	139.5	147.8	152.8	149.8	142.9	152	155.6	158.9	162.6	163.9	167.8
80	100	125.7	131.5	139.4	136.1	133.5	138.9	140.3	144.5	146.5	149.9	152.7
145	170.2	194.9	207.8	203	211.3	215.2	220.3	221.5	225	227.3	226	233.5
146	174.9	201.5	207.7	218.7	208.9	209.4	219.5	216.8	229.8	226	232.3	234.9
147	172.3	201.1	217.6	221.4	222.4	210	210.8	217.5	220.2	228.4	230.6	230
148	166.4	184.8	203.5	213.1	209.3	211.8	222.5	220.3	224.4	229.8	233	239.1
149	167.8	190	196.5	185.1	197.7	192.7	196.8	198	203.4	202.9	201.1	207.6
150	172.3	190.7	203.1	199.7	206.9	207.2	212.8	210.2	217.3	220.4	227.1	237.1
151	171.3	197.4	209	200.9	220.7	214.8	224.1	222	230.2	237.2	234.3	244.4
152	170.2	189.6	200.3	198.9	202.2	206.8	204.8	211.2	212.6	214.1	209.3	216
153	166.4	193	202.6	204.5	205.8	202.4	212.2	213.1	225.7	224	232	233.5
154	175.6	198.4	206.3	214.3	212.7	216.6	216.1	218.8	217.9	224.4	224.6	231.6
155	174.4	196.8	201.3	206.9	202.2	209.8	207.9	214.5	219.8	223.5	223.7	226.8
156	172.3	204.8	203.4	218.7	209.7	222.7	219.9	230.8	233.4	233.8	235.7	232.5
157	175.2	194.9	203.2	215.5	207.9	209	220.4	221.8	230.5	233	239.1	239.2

Animal	8/29/06	9/5/06	9/11/06	9/13/06	9/15/06	9/18/06	9/20/06	9/22/06	9/25/06	9/27/06	9/29/06	10/2/06
						Expo. day 0						Expo. day 14
158	171.6	205.1	211.2	217.7	215.1	219.3	228.5	227.3	235.4	235.3	239	244
159	171.9	209.7	205.7	216	218	219.9	226.4	230.3	233.5	236.1	235.6	242.4
160	179.4	204.7	203.1	216.3	206.9	219	222.7	229	232.7	237.7	237.6	239.4

Table 39. Body Weights of Naïve Rats (cont'd)

Animal	10/3/06	10/4/06	10/6/06	10/11/06	10/13/06	10/16/06
	Necropsy 1					Necropsy 2
65	151.5					
66	150.8					
67	165					
68	158.1					
69	163.4					
70	162.5					
71	167.7					
72	157.8					
73	153.8	148.8	150.7	150.1	150.8	159.1
74	150.9	147.6	147.9	149.4	148.8	155.8
75	154.5	152	152.3	154.7	153.9	166.6
76	161.5	155.9	156.7	158.6	157.5	167.1
77	165.3	156.5	161.7	159.1	157.4	162
78	162.4	155	157.2	163.1	164.5	166.9
79	167.7	164.6	164.1	164.5	163.4	167.9
80	155.2	148.7	153	154.2	154.6	161.3
145	230.7					
146	236.6					
147	226.7					
148	237.5					
149	206					
150	228.5					
151	244.6					
152	211.7					
153	237.1	224.5	229.3	232.3	231.2	236.7
154	226.6	228.3	224.5	225.3	231.1	228.8
155	231.9	225.7	226.9	232.6	234.8	244.5
156	234.7	232.6	230.2	235.5	232.2	241.4
157	241.3	234.2	236.6	243	241.3	249.9
158	242.4	239.1	245.9	248.5	248.9	251.9
159	239.8	231.4	235.4	237.1	239.6	243
160	245.1	240.9	240.1	250.8	244.9	253

Table 40. Body Weights of Air Exposed Rats

Animal	8/29/06	9/5/06	9/11/06	9/13006	9/15/06	9/18/06 Expo. day 0	9/20/06	9/22/06	9/25/06	9/27/06	9/29/06	10/2/06 Expo. day 14
1	112.1	125.4	126	133.5	132.8	136.7	129.8	138.1	135.6	140.8	139.4	143.2
2	112.1	135.2	145.3	148.6	149.9	156.3	147.6	147.5	146.8	151.2	152.1	153.3
3	105.7	126.6	135.7	138.3	138.8	143.2	140.2	141.7	144	145.1	145.9	145.5
4	111.5	129.3	143.4	147.2	143.4	140.9	145.5	145.4	144.2	150.7	150	152.2
5	117	138.2	149.8	157.4	154.5	147.9	150.3	150	154	150	153.1	152.3
6	103.3	128.5	122.2	142.9	138.5	138.5	134.9	137.2	138.2	144.3	144.5	145.8
7	112.9	135.3	145	142.9	146.1	149.8	144.1	148.3	149.4	152	151.9	155.4
8	105.2	127.2	131.4	134.8	133.7	134.2	132.8	132.4	135.9	136.2	138.5	139.5
33	108.2	127.1	138	146.7	144.4	153.4	143.8	149.8	149.4	152.5	152.9	154.3
34	116.2	133.8	141.4	145.9	144.9	151.4	145.2	143.7	148.1	145.4	150.4	147.3
35	103.2	121.4	134.4	135.3	135.8	130.4	135.4	139.4	139	140.4	142.2	145
36	119.9	135.5	138.4	150.6	149.8	151.7	150.9	149.1	153.9	151.4	156.4	155.2
37	109	132.6	144.7	150.4	150	147.4	149.5	147.2	156.7	152.6	153.8	160.1
38	100.5	117.1	122.2	128.1	127.7	130.7	129.6	131.3	134.6	138.4	140.3	144.1
39	105.9	127.5	140.1	139.3	138.5	133.8	138	135.8	142	141.5	143.4	142.8
40	106.1	124.8	123.6	140.5	138	139.6	138.1	134.2	142.6	142	143.2	144.3
81	182.1	225.3	240	243.5	241.7	240.9	239.3	235.4	248.8	252	251.1	255.7
82	196.2	227.2	226.8	235.8	212.9	225.9	215.8	213	221.9	215.3	224.2	226.1
83	198	226.2	243.1	244.3	245.3	245.3	233.5	243.3	246.2	251.2	247.6	248
84	190.2	211.3	212.1	221.8	225.9	217.9	213.4	223.9	225.9	230.7	228.8	230.5
85	194	221	226.6	244.3	228.7	229.7	229.5	233.5	238.6	229.7	239.6	243
86	187.2	213.8	217.3	231.3	225.5	228.9	222.1	236.4	229.3	233.8	227.2	241
87	171.2	196.9	203.9	218.8	207.3	215.9	213.1	213	220.5	216.9	222.6	224.3
88	166.2	197.5	213.2	212.1	213.7	216.6	215.1	213.7	211.2	222.5	215.2	225.6
113	183	220.2	219.7	237.9	226.4	236	224.7	236.9	243.9	239.8	248.3	252
114	181.9	201.3	192	212.2	212.1	213.8	205.6	210.3	212	207.4	213.5	219.5
115	174	203	219.7	219.9	225.3	226.9	224.2	226.6	225.6	238.7	233	241.7
116	173	205.4	224.6	228.8	225.9	234	223.1	223.2	229.5	231.9	237.2	233.4
117	174.3	204.5	221.6	220.4	225.2	216.3	222.4	222.1	222.8	232.4	229	239.5
118	169.8	208.2	219.6	237.2	226.4	240.8	234.8	236.6	243.1	234.7	241.8	246.4
119	175.2	203.7	207.5	218.3	208	205.2	206.3	204.4	211.8	207.5	209.5	212.9
120	162	192	212.6	213.8	213.1	221.4	211.7	210.6	208.1	219.5	214.3	227

Table 40. Body Weights of Air Exposed Rats (cont'd)

Animal	10/3/06 Necropsy 1	10/4/06	10/6/06	10/11/06	10/13/06	10/16/06 Necropsy 2
1	146.3					
2	158.3					
3	151.2					
4	153.1					
5	161.4					
6	149.6					

Animal	10/3/06	10/4/06	10/6/06	10/11/06	10/13/06	10/16/06
	Necropsy 1					Necropsy 2
7	158.1					
8	144.3					
33	160.5	164.7	167	167.7	174.7	159.1
34	153.3	159.2	164.2	165.7	166.2	163.2
35	150.5	152.3	154.7	159.6	156.6	155.9
36	160.5	168.6	168.5	172.8	170.7	170.5
37	161.8	166.7	169.7	165.6	165.7	171.9
38	148.5	152.6	155.9	154.5	155	154.2
39	148.2	151.9	155	159.3	161.4	155.6
40	148.3	154.1	152.7	154.8	146.4	156.2
81	265.4					
82	240.2					
83	259.2					
84	237.9					
85	250.1					
86	246					
87	237.1					
88	227.8					
113	262.7	265.2	275	280.3	262.2	273.4
114	224	239.7	251.3	251.9	231.9	243.4
115	234.5	268.1	264.5	256.8	263.7	259.8
116	244.5	254.3	252.3	258.9	270	261.3
117	241.7	258.7	257.5	253.7	265.9	259.4
118	255.9	260.5	263.7	268.6	259.9	265.4
119	219.2	209.7	227.6	233.7	239.7	227
120	228.3	245.4	241.7	244.4	247.9	239.4

Table 41. Body Weights of Low Concentration Rats

Animal	8/29/06	9/5/06	9/11/06	9/13006	9/15/06	9/18/06	9/20/06	9/22/06	9/25/06	9/27/06	9/29/06	10/2/06
						Expo. day 0						Expo. day 14
9	108.4	131.9	142.4	143	143	140.1	142	142.4	144.8	149.6	147	149.6
10	107.5	128.8	136.5	141.9	141.6	145	141.5	140.2	143.7	143.7	125.7	146.2
11	99.6	125	138	139.2	139.3	144.5	140.4	141.3	145.2	143.8	149.7	148.9
12	102.7	123	137.2	139.6	140	121.3	131.9	137.7	143.3	144.6	117.8	147.9
13	94.4	116.5	131	135	137.1	140	138.8	134.5	141.2	137.4	142.1	139.7
14	103.2	123.7	136.4	130.9	139.4	143.7	138.6	139.2	139.7	143.9	142.6	146.1
15	101.6	119.5	133.9	132.1	134.8	137	134.9	134.3	139.8	140.9	142.6	142.1
16	110.4	134.6	128.4	151.7	148.1	152.6	150.3	148.3	153.4	153.9	153.2	156.9
41	102.8	125.9	135.9	141.8	140.3	149.8	139.6	141.4	144.1	142.2	143.9	143.6
42	97.5	122.3	135.7	143.3	139.6	140.7	138	136.7	144.7	142.7	147	143.6
43	101	123.1	141.1	144.6	142.1	146.9	*141.5*	*162*	146.2	148.7	147.1	147.3
44	102.6	126.4	139.3	143.2	143.1	136.9	142.3	144.8	149.3	147.1	148.8	152
45	103.2	128.5	144.1	145.5	141.5	147.3	143.1	143.8	149.1	153.3	150.1	155.4

Animal	8/29/06	9/5/06	9/11/06	9/13006	9/15/06	9/18/06	9/20/06	9/22/06	9/25/06	9/27/06	9/29/06	10/2/06
						Expo. day 0						Expo. day 14
46	99.5	123	131.3	133.5	134.7	135.6	133.1	136.7	138.7	142.8	130	144.5
47	104.7	124.4	136	139.4	137.3	141.1	134.6	138.5	144.8	147.5	147.9	147.6
48	107.5	131.6	133.3	146.7	142.3	146.7	141.5	142.6	147	148.3	151.3	149.8
89	171.2	192.1	192.6	203.4	199.3	199.6	200.4	190.8	201.4	200.8	205.2	208.5
90	171.3	206	204.6	225.4	214	224.8	221.1	227.8	233.5	234.1	245.9	246.3
91	172	205.5	212.7	223.7	211.3	215.9	213.3	216.3	218.6	217.3	219.4	222.9
92	165	182	179.7	198.7	206.8	190.2	186.9	192	192.4	186.5	194.8	197.6
93	164.4	202.7	211.6	215.7	211.1	214.5	218.2	211	214.3	213.2	217.5	219.5
94	170.2	192.7	210.1	205.2	216.7	216.9	205.6	209.8	219.2	201.1	224.4	221.2
95	176	223.4	232.4	247.3	237.1	254	243.5	251.2	254.3	189.2	260.6	263.4
96	169	194.8	198.7	207.1	198.2	209.5	204.4	204.7	208.8	186.1	210.9	214.2
121	179.2	203.1	211.2	217.8	216.9	209.6	207.9	203.5	218.3	209.4	222.4	217
122	171.4	200.3	215.6	224.6	228.4	229.3	222.5	223	224.5	232.5	230.4	241.5
123	167.2	202.4	216.5	219.9	218.4	217.5	218.6	217	217	224.2	221.6	218.6
124	166	205.1	215.6	225.1	219.6	218.9	218.4	219.2	225.2	219.6	229.6	227.8
125	167.5	197.9	208.7	218.1	215.8	213.3	209.2	207.1	217.4	217.7	219.5	221.7
126	193	223.1	239.8	240.9	242.5	246.4	237.7	244.4	241.9	246.9	247.8	242.6
127	169.2	197.9	204.8	210.2	207	204.1	202.9	201.5	214.3	211.6	215.9	230.8
128	177	218.8	238	246.8	243.9	241.9	244.3	245.6	247	249.4	257.9	259.6

Table 41. Body Weights of Low Concentration Rats (cont'd)

Animal	10/3/2006	10/4/2006	10/6/2006	10/11/2006	10/13/2006	10/16/2006
	Necropsy 1					Necropsy 2
	156.1					
10	153.4					
11	152.6					
12	154.3					
13	150.1					
14	151.3					
15	150.4					
16	162.4					
41		151.1	152.2	157.8	161.1	184.6
42		154.5	158.5	160	159.8	159.3
43		156.3	157.4	166.8	168.2	165.8
44		156.4	156.5	159.7	161.2	151.5
45		162.9	164.9	166.6	168.7	149.1
46		153.1	152.7	157	153.9	142.7
47		158.2	160.4	167.7	167.1	168.3
48		160.2	164.4	160.8	166.4	167.4
89	223.3					

Animal	10/3/2006	10/4/2006	10/6/2006	10/11/2006	10/13/2006	10/16/2006
	Necropsy 1					Necropsy 2
90	260.1					
91	229.2					
92	212.9					
93	234.1					
94	231.5					
95	273.8					
96	228.5					
121		230.7	235.5	249.4	250.7	238.9
122		265.6	257.2	258.3	263.6	263
123		228.1	235.5	240.5	242.1	236
124		248.5	240.1	248.2	257.7	263.9
125		232.4	243.2	244.9	245.2	242.7
126		268	253.9	270.6	270.5	270.1
127		248.3	247.1	236.3	249.3	249.5
128		266.7	280.5	284.4	284.1	278.6

Table 42. Body Weights of Medium Concentration Rats

Animal	8/29/06	9/5/06	9/11/06	9/13006	9/15/06	9/18/06	9/20/06	9/22/06	9/25/06	9/27/06	9/29/06	10/2/06
						Expo. day 0						Expo. day 14
17	109.9	134	137	137.7	139.9	150.4	145.5	147.4	147.7	119.5	151.4	151.8
18	113.4	125.8	131.7	136.5	135.6	142.3	134.1	137.4	135	142.8	140.9	142.3
19	107.5	130.4	140.6	146.6	142.4	146.6	140.5	145.1	146.1	148.6	150.3	150.8
20	118.2	137.1	146.8	151	150.6	154.6	145.5	147.8	150.2	133.4	146.5	151.6
21	110.7	127.2	137.2	143.1	143.9	147.4	141.9	140.1	142.5	142.1	144.3	144.9
22	116	139.3	149.8	156.7	155.4	154.6	154.4	153.5	153.5	161.3	156.5	159.9
23	102.8	125.5	135.3	141.2	138.4	142	140.1	139.2	141	145	145.1	146.7
24	104.7	123.6	136.6	139.3	139.9	142.2	136.6	139.7	139.8	138.4	139.2	143
49	100.3	119	134.9	136.1	135.7	136	130	134.1	135.4	136.7	133	135.4
50	99.3	123.6	134.6	142.3	136.9	143.2	138.8	137.4	143	143.5	143.4	148.2
51	101.3	123.4	130.7	133.9	136.2	134.7	127.6	129.2	134	133.9	133.5	138.5
52	107.3	125.1	132.5	133.3	133.4	132.6	130.9	133.9	137.1	142.9	137.2	141
53	101.2	123.1	132.1	134	134.7	138.1	133.3	135.9	135.2	137.3	137.5	139.2
54	105.2	127.6	135.9	140.2	138.8	143.1	134.5	139.8	136.9	141.4	141.2	142.2
55	103.2	126.6	124.2	137.8	139.7	141.5	136.3	136.4	138.8	135.8	140.9	139
56	112.5	130.1	138.9	140.6	142.9	139.6	136.8	138.2	139.2	140.1	138.3	141.6
97	172.3	206.9	219.6	219.1	229.4	224	217.7	217.1	212.7	221.6	218.5	228.5
98	190.2	220.1	232.9	242.1	241.3	241.3	239.7	238.4	241.3	237.4	244.3	247.4
99	172	207.1	218.5	229.5	220.6	218.7	221.2	216.8	229.1	231.1	230.3	233.1
100	168	199.6	195.9	208.8	202.2	211.2	205.5	203.4	208.4	202.2	215.8	214.8
101	169.2	206.1	218.7	230.3	236.8	230.1	203.2	224	232.5	231.9	240.7	243.2

Animal	8/29/06	9/5/06	9/11/06	9/13006	9/15/06	9/18/06	9/20/06	9/22/06	9/25/06	9/27/06	9/29/06	10/2/06
						Expo. day 0						Expo. day 14
102	170.4	203.2	212.1	185.7	216.7	204.9	217.8	209.6	215	219.2	223.9	229.9
103	167.4	198.3	205.3	211.5	204.7	206.8	199.5	202.8	205.8	201.4	209.3	208.7
104	182.5	208.8	212.3	220.4	208.8	219.5	207.2	205.9	209.2	214.6	217.2	214.1
129	171.4	201.7	211.7	209.4	207.8	209.8	203.8	202.1	214.9	203.8	217.4	211.1
130	173	208.8	203.1	219.2	205.1	211.5	211	212.3	218.4	213.4	220.1	223.7
131	166.2	198.4	216.2	224	214.4	223.4	211.9	211.3	219.6	212.3	221.1	221
132	169.9	199.2	207.6	200.2	231.9	209.7	205.7	206	203.3	211	211.3	215.5
133	169.4	209.8	218.9	226.2	216.6	229.7	216.8	219.1	219.7	218.3	223.4	225.9
134	172.4	217.6	235.2	235.5	236.9	238.7	238.5	232.2	229.6	242.9	235.5	245.6
135	174.2	195.3	202.1	207.6	209.1	205.8	210.8	210.5	222	219.6	213.4	224.1
136	170.3	189.9	196.2	212.3	197.6	206	196.8	201.8	206.5	199.9	206.6	211.7

Table 42. Body Weights of Medium Concentration Rats (cont'd)

Animal	10/3/06	10/4/06	10/6/06	10/11/06	10/13/06	10/16/06
	Necropsy 1					Necropsy 2
17	156.9					
18	148.9					
19	157.1					
20	154.6					
21	150.7					
22	165.7					
23	154.3					
24	148.9					
49		140.5	143.6	152.3	149.7	153.2
50		153.2	155.2	160.2	159.9	161.7
51		145.7	152	160.3	160.8	157.7
52		148.1	150.9	157.3	154.5	155.1
53		144.8	148.9	151.4	152.8	149.8
54		148	148.6	155.4	155.9	156.4
55		148.3	152.2	158.2	159.6	157.6
56		151.4	152.3	160.2	162.5	161.5
97	237.5					
98	259.8					
99	241.8					
100	223.4					
101	257.1					
102	243.3					
103	221.2					
104	218.5					
129		229.7	227.3	240.7	236	237.7

Animal	10/3/06	10/4/06	10/6/06	10/11/06	10/13/06	10/16/06
	Necropsy 1					Necropsy 2
130		236.4	238.5	244.2	234.8	246.2
131		239.9	237.7	246	241.3	242.4
132		225.7	231.3	239.3	236.5	231.6
133		244.3	248.4	254.9	245.5	248.5
134		264.3	264.5	260	275.6	269.8
135		234.5	239.5	236.1	247.5	241.7
136		224.2	228	225.3	219.9	240.1

Table 43. Body Weights of High Concentration Rats

Animal	8/29/06	9/5/06	9/11/06	9/13006	9/15/06	9/18/06	9/20/06	9/22/06	9/25/06	9/27/06	9/29/06	10/2/06
						Expo. day 0						Expo. day 14
25	107.4	123.7	133	116.6	136	139.8	131.7	131.5	132.2	133.8	133.1	135.1
26	98.9	123.5	126.8	130.8	135.5	142.2	133.4	133.7	135.8	133.7	137.9	135.2
27	90.2	114.8	123.4	129	126.4	129.5	122.5	121.2	119.5	123.2	126	127
28	104.2	128.3	130.2	139.4	138.4	144.8	134.6	135.7	136.6	140.8	138.9	142
29	105.4	129.2	138.9	142.1	140.6	146.7	137.2	136.6	136.9	137.9	139.2	138.5
30	103.8	121.2	129.9	135.3	131.4	127.4	128.2	129.4	130.6	136.2	135.4	134.9
31	96.8	115.7	123.5	125.1	127.9	130.2	119.5	129.9	122.2	123.1	122.7	124.6
32	109.4	128.8	134	139.8	142.2	144.9	136.3	138.7	139.3	142.2	140.8	140.3
57	100.1	124.4	140.6	143	143.2	145.7	136.6	134.3	137.5	139.5	141.6	142.4
58	104.2	126.6	136.4	141.6	141.7	142.8	137.3	133.5	139.4	141.9	142.3	141.3
59	102.1	122.9	124.6	134.6	135	135.2	126.5	128	129.8	129.3	132.3	133.7
60	102.3	121.7	135.2	139.5	138.2	145.2	135.4	139.2	140.1	142.5	140.6	139.8
61	102.9	125.2	131.3	136.4	136.9	136.9	128.1	124.4	127.3	124.6	127.6	129.8
62	105.8	128.1	132.1	136.1	136.6	135.5	130.2	127.5	130.2	131.3	132	134.9
63	101.2	124.9	128.3	139.6	140.3	139.2	133	127.9	130.4	131.2	132	133.2
64	98.4	121.1	126.4	131.4	130	136	127.8	127.3	129.5	132.4	131.4	133
105	170.5	204.1	210.2	210.6	211.6	209.7	199.6	195.4	203.3	198.2	189.2	203.6
106	180.5	212.2	22.7	235.7	226.9	238.5	233.4	230.7	233.2	229.8	222.7	239.3
107	184.2	212	226.5	231.2	233.3	233.3	227.7	222.5	228.2	226.9	225.5	230
108	186	214.6	229.6	227.5	226.7	226.1	216.7	210.6	212.5	210.2	208.6	216.6
109	166	201.1	201.5	213.9	207.7	206.2	206.9	205.4	212.5	210.8	203	215.7
110	190	217.7	220.3	229.8	228.2	228.3	204.8	217	218.4	222.5	209.3	224
111	192.9	226.8	236.6	249.7	241.4	236.1	238.4	224.4	231.7	220.2	221.9	239.2
112	194.1	248.7	246.2	260.7	250.8	254.8	240.8	244.5	245.4	248.3	243.3	261.9
137	170.5	199.4	223.9	215.5	222.2	222.6	218.8	216.8	219	221.5	215.5	229
138	169.3	212	213.9	207.5	224.9	216.8	211	204.6	207.1	204.1	192.9	213.8
139	189.2	213.1	221.1	224.1	220.4	222.8	220.1	218.3	222.2	212	224.8	233.1
140	174.8	204.2	218.8	217.4	212	223.9	217	217.4	218.8	229.5	225.1	232.4
141	190.4	233.5	203.5	210.9	209.4	202.5	198.8	198.2	206.3	197.5	204.9	203.4

Animal	8/29/06	9/5/06	9/11/06	9/13006	9/15/06	9/18/06	9/20/06	9/22/06	9/25/06	9/27/06	9/29/06	10/2/06
						Expo. day 0						Expo. day 14
142	204.1	202.5	249.1	240.7	248.4	245	237.3	236.4	236.3	242	231.3	239.7
143	181.3	210.2	208.2	220.9	210.8	218.3	209.3	210.9	211.7	216.1	216.7	219.9
144	188.5	207	214.6	222.7	231.6	224.4	212.2	216	223.1	231.2	234.5	229.1

Table 43. Body Weights of High Concentration Rats (cont'd)

Animal	10/3/06	10/4/06	10/6/06	10/11/06	10/13/06	10/16/06
	Necropsy 1					Necropsy 2
25	143.1					
26	144.5					
27	135					
28	149.6					
29	147.9					
30	141.8					
31	137.7					
32	148.9					
57		151.4	151.2	158.8	138.4	159.4
58		154.9	154.9	163.6	166.8	163.8
59		145.8	145.8	150.7	154.4	153.6
60		152	149.3	158.9	162	161.5
61		142.8	141.1	152.2	153.2	150.6
62		141.7	145	150.8	151	155.7
63		148.2	149.3	157.7	161.5	161.8
64		143.3	143.3	148.9	152.9	152.6
105	228.9					
106	263.3					
107	251.1					
108	232					
109	236.4					
110	245.1					
111	256.6					
112	284.3					
137		236	248.4	250	254.8	248.6
138		231.1	239.5	229.2	248.4	236.9
139		255	261.9	252.7	261.8	254.9
140		251.4	252.3	246.5	268.1	257.6
141		220.5	223.1	225.7	218.1	226.1
142		149	265.7	267.5	272.9	261.1
143		244.6	239.2	230.9	245.2	237.4
144		239.8	245.6	250	239.7	249.9

Organ Weights

Table 44. Organ Weights at Necropsy 24 hrs after the Final Exposure

		Organ Weight (g)						
Animal #	**Group**	Brain	Thoracic	Kidney	Spleen	Liver	GI tract	Sex
6	**Control F**	1.76	1.94	1.21	0.48	5.23	18.93	0.78
7	Control	1.77	2.08	1.25	0.39	5.57	17.82	0.98
8	C	1.60	1.91	1.27	0.45	5.15	15.18	1.32
86	**Control SD**	1.82	3.45	1.73	0.61	8.91	25.68	1.66
87	C	1.76	2.99	1.92	0.57	9.26	29.53	1.09
88	C	1.75	3.21	1.68	0.62	8.28	21.01	2.23
14	**Low F**	1.83	2.28	1.15	0.44	5.09	20.18	1.03
15	Low	1.63	2.15	1.30	0.41	5.65	17.09	0.90
16	L	1.66	2.27	1.34	0.47	6.14	20.22	1.31
94	**Low SD**	1.98	3.10	1.80	0.65	9.43	28.02	1.11
95	L	2.00	3.59	2.02	0.72	11.11	38.87	1.32
96	L	1.76	2.78	1.64	0.42	7.31	23.12	0.97
22	**Med F**	1.79	2.44	1.20	0.50	5.55	17.25	1.04
23	Med	1.40	2.40	1.32	0.39	5.78	18.79	0.69
24	M	1.72	2.54	1.21	0.35	5.11	15.26	1.16
102	**Med SD**	1.78	3.60	1.65	0.58	8.36	30.93	1.10
103	M		3.27	1.63	0.63	7.50	24.55	1.20
104	M	1.78	3.01	1.45	0.60	6.20	18.09	1.31
30	**High F**	1.66	1.99	1.20	0.46	5.50	17.77	0.53
31	High	1.63	2.08	1.13	0.52	4.70	16.55	0.74
32	H	1.76	2.53	1.24	0.55	6.10	18.70	0.75
110	**High SD**	1.67	3.48	1.70	0.64	8.30	23.70	1.36
111	H	2.00	3.72	1.77	0.72	10.44	33.10	1.02
112	H	1.80	3.79	2.17	0.74	12.24	37.95	1.11
70	**Naïve F**	1.62	2.20	1.12	0.39	6.15	18.83	0.79
71	Naïve	1.54	2.40	1.28	0.47	6.70	20.05	0.93
72	N	1.56	2.26	1.38	0.40	6.33	17.51	0.99
150	**Naïve SD**	1.63	3.09	1.83	0.61	9.06	22.74	1.46
151	N	1.62	3.03	1.65	0.60	8.82	22.43	1.73

Table 45. Organ Weights at Necropsy 14 days after the Final Exposure

		Organ Weight (g)						
Animal #	**Group**	Brain	Thoracic	Kidney	Spleen	Liver	GI tract	Sex
38	**Control F**	1.63	1.98	0.88	0.39	4.73	16.80	0.64
39	Control	1.67	2.08	1.52	0.37	5.43	19.64	0.78
40	C	1.73	1.92	1.45	0.37	5.10	15.55	0.38
46	**Low F**	1.91	1.98	1.51	0.30	5.45	18.34	1.04
47	Low	1.73	2.44	1.52	0.52	5.25	19.95	0.10
48	L	1.70	2.36	1.53	0.46	4.94	16.96	0.22
54	**Med F**	0.80	2.04	1.63	0.46	5.96	16.89	0.84
55	Med	1.31	2.26	1.55	0.45	5.16	16.15	1.41
56	M	1.73	2.22	1.53	0.44	5.34	18.68	0.56
62	**High F**	1.73	1.91	1.58	0.40	4.99	17.10	0.77

		Organ Weight (g)						
Animal #	**Group**	Brain	Thoracic	Kidney	Spleen	Liver	GI tract	Sex
63	High	1.84	1.80	1.65	0.47	5.81	20.45	0.93
64	H	1.82	1.97	1.58	0.52	5.92	17.86	1.14
78	**Naïve F**	1.41	2.36	1.34	0.42	6.14	19.39	0.59
79	Naïve	1.86	2.39	1.02	0.49	5.27	19.40	0.78
80	N	1.29	2.16	1.25	0.25	5.56	17.38	1.26
118	**Control SD**	1.94	3.40	2.29	0.25	8.55	27.68	1.27
119	C	1.75	2.03	1.88	0.65	7.20	17.82	1.83
120	C	1.73	3.50	1.83	0.48	7.05	25.70	1.35
126	**Low SD**	2.01	2.41	2.14	0.93	9.80	28.23	0.20
127	L	2.14	3.05	1.91	0.57	8.19	21.41	0.34
128	L	1.02	3.36	2.16	0.63	8.61	20.26	7.63
134	**Med SD**	1.73	3.27	2.24	0.93	9.55	29.64	1.44
135	M	1.96	3.07	2.08	0.44	9.40	23.44	1.43
136	M	1.88	3.29	1.83	0.71	9.09	25.58	1.51
142	**High SD**	1.74	1.96	2.10	0.62	8.40	19.99	2.22
143	H	1.94	2.65	1.98	0.63	7.73	18.40	1.12
144	H	1.76	2.68	1.89	0.79	8.33	23.18	1.53
158	**Naïve SD**	1.84	2.93	0.75	0.73	8.40	22.70	1.86
159	N	1.83	3.19	1.19	0.59	7.61	18.75	1.30
160	N	1.64	2.40	1.31	0.40	8.99	24.33	0.96

CBC with Differential (Charles River Laboratories)

Table 46. CBC 24-hrs after Final Exposure

Animal number	**6**	**7**	**8**	**14**	**15**	**22**	**23**	**24**
WBC ($x10^3$/µl)	4.32	3.25	3.54	3.43	3.98	2.61	4.48	3.93
RBC ($x10^6$/µl)	8.74	8.61	9.00	8.63	9.04	8.67	8.75	8.56
HGB (g/dl)	16.5	16.2	17.1	15.9	16.9	16.2	16.5	15.9
HCT (%)	48.7	48.4	50.3	47.1	51.9	46.6	49.3	47.3
MCV (fL)	55.7	56.2	55.9	54.6	57.4	53.8	56.3	55.3
MCH (pg)	18.9	18.8	19.0	18.4	18.7	18.7	18.9	18.6
MCHC (g/dl)	33.9	33.6	34.1	33.7	32.6	34.7	33.6	33.7
CHCM (g/dl)	32.6	32.4	32.4	32.5	31.1	33.7	31.9	32.8
CH (pg)	18.1	18.1	18.0	17.7	17.8	18.0	17.9	18.0
RDW (%)	11.2	11.7	11.7	11.6	11.6	11.4	11.6	11.7
HDW (g/dl)	2.59	2.45	2.51	2.33	2.35	2.60	2.32	2.47
PLT ($x10^3$/µl)	781	814	713	781	791	782	783	752
MPV (fL)	8.6	8.4	8.7	8.6	9.9	8.3	8.8	9.0
% NEUT	13.7	14.7	16.0	19.6	15.2	16.9	17.3	19.6
% LYMPH	77.2	75.6	76.4	73.1	78.2	74.4	76.0	71.6
% MONO	1.3	2.0	1.0	1.5	1.4	1.2	1.5	1.7
% EOS	2.1	1.6	1.4	2.2	0.8	1.9	1.1	2.1
% BASO	4.7	4.7	3.9	2.6	3.3	4.6	3.1	4.0
% LUC	0.9	1.4	1.3	0.9	1.2	1.0	1.0	1.0
#NEUT ($x10^3$/µl)	0.59	0.48	0.57	0.67	0.60	0.44	0.78	0.77
#LYMPH ($x10^3$/µl)	3.33	2.46	2.70	2.51	3.11	1.94	3.41	2.81
#MONO ($x10^3$/µl)	0.06	0.06	0.04	0.05	0.06	0.03	0.07	0.07

Animal number	6	7	8	14	15	22	23	24
#EOS (x10^3/µl)	0.09	0.05	0.05	0.08	0.03	0.05	0.05	0.08
#BASO (x10^3/µl)	0.20	0.15	0.14	0.09	0.13	0.12	0.14	0.16
#LUC (x10^3/µl)	0.04	0.05	0.04	0.03	0.05	0.03	0.05	0.04

Table 46. CBC 24-hrs after Final Exposure (cont'd)

Animal number	30	31	70	71	72	86	94	95
WBC (x10^3/µl)	4.43	4.81	4.74	6.00	4.79	1.73	5.91	3.86
RBC (x10^6/µl)	8.69	8.56	8.31	8.68	8.91	7.24	7.96	7.39
HGB (g/dl)	16.6	16.2	15.5	16.3	16.8	14.3	15.6	15.8
HCT (%)	49.2	46.9	45.5	48.6	50.9	43.7	46.2	45.6
MCV (fL)	56.6	54.8	54.8	56.0	57.1	60.3	58.1	61.6
MCH (pg)	19.1	18.9	18.7	18.8	18.8	19.8	19.6	21.4
MCHC (g/dl)	33.7	34.4	34.1	33.6	32.9	32.8	33.7	34.7
CHCM (g/dl)	31.5	32.4	32.5	32.3	31.5	32.0	31.6	32.5
CH (pg)	17.8	17.7	17.7	18.0	17.9	19.2	18.3	20.0
RDW (%)	11.5	11.4	11.4	11.8	11.4	13.1	11.7	11.1
HDW (g/dl)	2.36	2.47	2.52	2.51	2.32	2.44	2.32	2.42
PLT (x10^3/µl)	788	770	754	720	780	804	958	1117
MPV (fL)	9.7	9.1	8.4	8.7	9.5	8.5	9.4	9.0
% NEUT	15.8	12.9	10.9	12.4	11.5	13.7	11.1	8.1
% LYMPH	74.9	83.3	84.0	79.9	82.3	78.8	84.8	87.2
% MONO	1.8	1.5	1.2	1.4	1.5	1.7	0.8	1.0
% EOS	1.7	1.4	0.9	1.4	1.4	1.5	2.6	2.6
% BASO	4.8	4.9	2.8	4.3	2.2	3.1	6.3	6.5
% LUC	1.0	0.9	0.2	0.6	1.1	1.2	0.8	1.2
#NEUT (x10^3/µl)	0.70	0.62	0.49	0.75	0.55	0.24	0.66	0.31
#LYMPH (x10^3/µl)	3.32	4.01	3.76	4.79	3.94	1.36	5.01	3.37
#MONO (x10^3/µl)	0.08	0.07	0.05	0.09	0.07	0.03	0.04	0.04
#EOS (x10^3/µl)	0.07	0.07	0.04	0.08	0.07	0.03	0.15	0.10
#BASO (x10^3/µl)	0.21	0.24	0.13	0.26	0.11	0.05	0.37	0.25
#LUC (x10^3/µl)	0.05	0.04	0.01	0.04	0.05	0.02	0.05	0.04

Table 46. CBC 24-hrs after Final Exposure (cont'd)

Animal number	96	103	104	110	111	112	150	151
WBC (x10^3/µl)	3.60	3.44	1.75	5.43	4.05	3.80	4.32	3.90
RBC (x10^6/µl)	7.57	8.02	8.27	8.22	7.65	7.07	8.04	7.96
HGB (g/dl)	15.4	15.4	15.1	17.0	15.1	14.2	15.1	15.4
HCT (%)	46.1	43.2	43.1	52.3	45.3	41.9	44.3	44.8
MCV (fL)	60.9	53.9	52.1	63.6	59.3	59.3	55.1	56.3
MCH (pg)	20.4	19.2	18.2	20.7	19.7	20.0	18.7	19.3
MCHC (g/dl)	33.5	35.6	34.9	32.6	33.3	33.8	34.0	34.2
CHCM (g/dl)	31.2	33.2	33.9	29.7	31.1	31.0	33.0	33.4
CH (pg)	18.9	17.8	17.6	18.8	18.4	18.3	18.1	18.7
RDW (%)	11.8	11.9	12.0	11.6	11.2	11.7	12.9	12.4
HDW (g/dl)	2.25	2.58	2.43	2.04	2.49	2.19	3.31	2.82
PLT (x10^3/µl)	947	865	864	854	1024	978	1017	897
MPV (fL)	9.3	9.2	7.9	12.1	9.4	9.7	8.4	8.7
% NEUT	11.8	12.5	18.3	20.4	9.8	12.2	9.8	11.3

Animal number	96	103	104	110	111	112	150	151
% LYMPH	82.6	79.3	77.9	71.5	81.2	79.9	86.1	84.4
% MONO	1.0	1.0	1.0	1.1	1.2	1.3	1.3	0.9
% EOS	3.4	4.6	0.8	1.4	1.8	1.4	1.8	2.1
% BASO	5.9	2.0	1.4	4.8	4.3	4.1	0.6	1.0
% LUC	1.3	0.6	0.7	0.8	1.8	1.3	0.3	0.3
#NEUT ($x10^3$/µl)	0.42	0.43	0.32	1.11	0.40	0.46	0.43	0.44
#LYMPH ($x10^3$/µl)	2.98	2.73	1.36	3.88	3.29	3.03	3.72	3.29
#MONO ($x10^3$/µl)	0.04	0.03	0.02	0.06	0.05	0.05	0.06	0.03
#EOS ($x10^3$/µl)	0.12	0.16	0.01	0.07	0.07	0.05	0.08	0.08
#BASO ($x10^3$/µl)	0.21	0.07	0.02	0.26	0.18	0.16	0.03	0.04
#LUC ($x10^3$/µl)	0.05	0.02	0.01	0.04	0.07	0.05	0.02	0.01

The sample for animal 87 was clotted and unable to be analyzed.

Table 47. CBC 14-Days after Final Exposure

Animal number	38	39	40	47	48	55	56	62
WBC ($x10^3$/µl)	3.15	2.52	3.05	2.93	3.32	2.83	3.13	3.07
RBC ($x10^6$/µl)	8.50	7.90	7.76	8.12	8.34	8.02	8.00	7.10
HGB (g/dl)	16.1	14.9	14.5	15.5	16.0	15.7	15.0	13.6
HCT (%)	46.8	42.1	40.9	45.2	47.1	44.6	42.6	36.9
MCV (fL)	55.0	53.2	52.7	55.6	56.5	55.6	53.2	52.0
MCH (pg)	19.0	18.8	18.7	19.1	19.2	19.6	18.8	19.2
MCHC (g/dl)	34.5	35.4	35.5	34.3	33.9	35.2	35.2	36.9
CHCM (g/dl)	33.0	34.3	34.7	32.7	31.7	32.2	34.0	35.2
CH (pg)	18.0	18.2	18.2	18.1	17.8	17.8	18.0	18.3
RDW (%)	12.4	12.2	12.4	12.2	12.1	12.5	13.3	12.7
HDW (g/dl)	2.59	2.67	2.68	2.39	2.39	2.53	2.75	2.83
PLT ($x10^3$/µl)	757	679	680	73	624	710	601	662
MPV (fL)	8.0	7.8	7.6	9.0	8.4	8.6	7.9	7.7
% NEUT	15.3	14.5	11.2	11.2	13.7	12.9	9.8	9.3
% LYMPH	75.1	76.8	79.7	80.1	74.3	79.2	81.0	84.0
% MONO	7.9	6.5	7.2	5.2	7.1	5.9	6.4	5.0
% EOS	0.5	0.9	0.6	0.4	0.2	0.5	0.4	0.5
% BASO	5.0	0.6	0.8	2.1	3.7	5.2	2.0	0.9
% LUC	1.2	0.6	0.6	1.0	1.0	1.4	0.4	0.2
#NEUT ($x10^3$/µl)	0.48	0.37	0.34	0.33	0.45	0.36	0.30	0.29
#LYMPH ($x10^3$/µl)	2.36	1.94	2.43	2.34	2.47	2.24	2.53	2.58
#MONO ($x10^3$/µl)	0.25	0.16	0.22	0.15	0.24	0.17	0.20	0.15
#EOS ($x10^3$/µl)	0.02	0.02	0.02	0.01	0.01	0.02	0.01	0.01
#BASO ($x10^3$/µl)	0.16	0.02	0.02	0.06	0.12	0.15	0.06	0.03
#LUC ($x10^3$/µl)	0.04	0.01	0.02	0.03	0.03	0.04	0.01	0.01

Table 47. CBC 14-Days after Final Exposure (cont'd)

Animal number	63	64	78	79	80	118	119	120
WBC ($x10^3$/µl)	3.85	3.71	4.52	5.07	6.06	3.41	1.06	2.59
RBC ($x10^6$/µl)	8.01	8.56	7.82	8.51	8.72	7.68	7.72	8.18
HGB (g/dl)	15.7	16.2	15.2	16.2	16.4	14.4	15.4	15.7

Animal number	63	64	78	79	80	118	119	120
HCT (%)	45.3	48.1	40.4	46.4	49.2	40.9	44.7	44.7
MCV (fL)	56.6	56.2	51.6	54.5	56.4	53.3	57.9	54.7
MCH (pg)	19.6	18.9	19.4	19.0	18.8	18.8	20.0	19.2
MCHC (g/dl)	34.7	33.6	37.5	34.9	33.4	35.3	34.6	35.2
CHCM (g/dl)	31.8	31.8	35.8	32.9	31.7	34.1	33.5	34.1
CH (pg)	17.9	17.8	18.4	17.9	17.8	18.1	19.3	18.6
RDW (%)	12.5	12.2	12.1	11.7	12.2	12.7	12.4	12.2
HDW (g/dl)	2.46	2.50	2.79	2.54	2.46	3.34	2.46	2.50
PLT ($x10^3$/µl)	630	733	566	731	689	1060	1030	794
MPV (fL)	8.9	8.5	7.5	8.2	8.5	7.6	7.7	7.9
% NEUT	12.6	12.2	9.2	10.4	10.1	4.5	16.2	11.3
% LYMPH	80.2	79.8	83.0	79.6	83.3	90.8	71.7	78.3
% MONO	5.6	6.0	6.2	5.6	5.0	2.2	7.8	6.1
% EOS	0.5	0.4	0.5	0.6	0.4	0.4	1.1	2.7
% BASO	9.2	7.6	0.6	3.0	9.1	1.6	2.9	1.6
% LUC	1.1	1.7	0.4	0.7	1.2	0.5	0.4	0.1
#NEUT ($x10^3$/µl)	0.48	0.45	0.42	0.53	0.61	0.15	0.17	0.29
#LYMPH ($x10^3$/µl)	3.09	2.93	3.75	4.03	5.05	3.10	0.76	2.02
#MONO ($x10^3$/µl)	0.22	0.22	0.28	0.29	0.30	0.07	0.08	0.16
#EOS ($x10^3$/µl)	0.02	0.01	0.02	0.03	0.02	0.01	0.01	0.07
#BASO ($x10^3$/µl)	0.35	0.28	0.03	0.15	0.55	0.06	0.03	0.04
#LUC ($x10^3$/µl)	0.04	0.06	0.02	0.04	0.07	0.02	0.00	0.00

Table 47. CBC 14-Days after Final Exposure (cont'd)

Animal number	126	127	128	135	136	142	144	158
WBC ($x10^3$/µl)	4.96	2.68	2.11	2.34	3.56	2.49	2.58	4.91
RBC ($x10^6$/µl)	8.00	7.59	7.84	7.99	7.31	7.46	7.67	7.95
HGB (g/dl)	14.9	15.1	15.5	15.6	14.8	15.2	14.8	15.9
HCT (%)	42.4	15.2	44.6	45.6	43.0	43.5	42.1	45.7
MCV (fL)	53.0	59.2	56.9	57.1	58.9	58.3	55.0	57.5
MCH (pg)	18.7	19.9	19.7	19.5	20.3	20.3	19.3	20.0
MCHC (g/dl)	35.2	33.4	34.7	34.1	34.4	34.9	35.1	34.8
CHCM (g/dl)	33.9	31.9	33.4	31.7	32.9	33.5	32.8	33.5
CH (pg)	17.8	18.9	18.9	18.0	19.3	19.4	18.0	19.2
RDW (%)	12.8	12.1	12.2	15.0	11.7	12.8	12.1	12.0
HDW (g/dl)	3.24	2.45	2.64	3.19	2.36	2.53	2.33	2.41
PLT ($x10^3$/µl)	846	707	777	822	813	854	650	595
MPV (fL)	7.4	8.2	8.1	8.6	8.0	7.6	7.8	8.6
% NEUT	5.1	11.2	11.8	7.2	8.8	5.9	13.2	19.4
% LYMPH	90.4	80.0	79.4	83.7	82.9	88.9	78.9	73.0
% MONO	2.5	6.7	6.9	3.2	6.5	3.5	6.1	4.8
% EOS	1.2	1.3	0.8	1.4	0.4	0.8	0.7	0.8
% BASO	0.7	0.8	0.6	3.9	0.8	0.7	1.0	1.6
% LUC	0.2	0.1	0.5	0.6	0.5	0.3	0.2	0.3
#NEUT ($x10^3$/µl)	0.25	0.30	0.25	0.17	0.31	0.15	0.34	0.95
#LYMPH ($x10^3$/µl)	4.48	2.15	1.67	1.96	2.95	2.22	2.03	3.59
#MONO ($x10^3$/µl)	0.12	0.18	0.14	0.07	0.23	0.09	0.16	0.24
#EOS ($x10^3$/µl)	0.06	0.03	0.02	0.03	0.02	0.02	0.02	0.04
#BASO ($x10^3$/µl)	0.03	0.02	0.01	0.09	0.03	0.02	0.03	0.08

Animal number	126	127	128	135	136	142	144	158
#LUC (x10^3/µl)	0.01	0.00	0.01	0.01	0.02	0.01	0.00	0.01

Table 47. CBC 14-Days after Final Exposure (cont'd)

Animal number	159
WBC (x10^3/µl)	4.59
RBC (x10^6/µl)	8.13
HGB (g/dl)	15.6
HCT (%)	44.5
MCV (fL)	54.7
MCH (pg)	19.2
MCHC (g/dl)	35.0
CHCM (g/dl)	33.4
CH (pg)	18.2
RDW (%)	11.8
HDW (g/dl)	2.50
PLT (x10^3/µl)	817
MPV (fL)	7.5
% NEUT	7.7
% LYMPH	83.5
% MONO	5.1
% EOS	1.0
% BASO	1.9
% LUC	0.8
#NEUT (x10^3/µl)	0.36
#LYMPH (x10^3/µl)	3.83
#MONO (x10^3/µl)	0.23
#EOS (x10^3/µl)	0.05
#BASO (x10^3/µl)	0.09
#LUC (x10^3/µl)	0.04

Lung Lavage Cell Differential

Table 48. Lung Lavage Cell Data at 24 hrs after the Final Exposure

	4 Quadrants/ 100 cells per quadrant counted				
1-control	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100
Q3	100	0	0	0	100
Q4	100	0	0	0	100
%	100.00%	0.00%	0.00%	0.00%	

2-control	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	98	0	2	0	100
Q2	99	0	1	0	100
Q3	100	0	0	0	100
Q4	100	0	0	0	100

	%	99.25%	0.00%	0.75%	0.00%	

3-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	98	0	2	0	100
	Q2	98	1	1	0	100
	Q3	98	0	2	0	100
	Q4	99	0	1	0	100
	%	98.25%	0.25%	1.50%	0.00%	

4-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

5-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

81-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

82-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

83-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

84-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	98	0	2	0	100
	Q4	100	0	0	0	100
	%	99.50%	0.00%	0.50%	0.00%	

85-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	99	1	0	0	100
	%	99.75%	0.25%	0.00%	0.00%	

9-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	0	1	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	99.75%	0.00%	0.25%	0.00%	

10-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	99	0	1	0	100
	Q4	100	0	0	0	100
	%	99.75%	0.00%	0.25%	0.00%	

11-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	1	0	0	100
	Q2	99	0	1	0	100
	Q3	97	2	1	0	100
	Q4	98	1	1	0	100
	%	98.25%	1.00%	0.75%	0.00%	

12-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	100	0	0	0	100
	Q3	99	0	1	0	100
	Q4	100	1	0	0	101
	%	99.25%	0.25%	0.50%	0.00%	

13-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	1	0	0	100
	Q2	98	1	1	0	100
	Q3	99	1	0	0	100
	Q4	98	0	2	0	100
	%	98.50%	0.75%	0.75%	0.00%	

89-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	96	1	2	1	100
	Q2	98	0	0	2	100
	Q3	98	0	2	0	100
	Q4	95	2	2	1	100
	%	96.75%	0.75%	1.50%	1.00%	

90-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

91-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	1	0	0	100
	Q2	98	1	1	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	99.25%	0.50%	0.25%	0.00%	

92-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

93-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	98	1	1	0	100
	Q3	99	0	1	0	100
	Q4	99	0	1	0	100
	%	99.00%	0.25%	0.75%	0.00%	

17-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	1	0	0	100
	Q3	100	0	0	0	100
	Q4	99	1	0	0	100
	%	99.50%	0.50%	0.00%	0.00%	

18-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	98	0	2	0	100
	%	99.50%	0.00%	0.50%	0.00%	

19-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	99.75%	0.00%	0.25%	0.00%	

20-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

21-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	99	0	1	0	100
	%	99.75%	0.00%	0.25%	0.00%	

97-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	98	0	2	0	100
	Q3	99	0	1	0	100
	Q4	100	0	0	0	100
	%	99.25%	0.00%	0.75%	0.00%	

98-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

99-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	0	1	0	100
	Q3	100	0	0	0	100
	Q4	99	0	1	0	100
	%	99.50%	0.00%	0.50%	0.00%	

100-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	98	1	1	0	100
	Q2	100	0	0	0	100
	Q3	99	1	0	0	100
	Q4	98	1	1	0	100
	%	98.75%	0.75%	0.50%	0.00%	

101-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	99	0	1	0	100
	Q3	98	1	1	0	100
	Q4	97	2	1	0	100
	%	98.25%	0.75%	1.00%	0.00%	

25-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	99	1	0	0	100
	Q3	99	0	1	0	100
	Q4	100	0	0	0	100
	%	99.25%	0.25%	0.50%	0.00%	

26-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	94	4	2	0	100
	Q2	95	4	1	0	100
	Q3	98	2	0	0	100
	Q4	97	2	1	0	100
	%	96.00%	3.00%	3.00%	0.00%	

27-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

28-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	98	2	0	0	100
	Q2	100	0	0	0	100
	Q3	98	2	0	0	100
	Q4	99	1	0	0	100
	%	98.75%	1.25%	0.00%	0.00%	

29-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	99	0	1	0	100
	Q3	97	2	1	0	100
	Q4	99	1	0	0	100
	%	98.50%	0.75%	0.75%	0.00%	

105-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	1	0	0	100
	Q3	99	0	0	1	100
	Q4	100	0	0	0	100
	%	99.50%	0.25%	0.00%	0.25%	

106-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	0	1	0	100
	Q3	98	1	1	0	100
	Q4	99	1	0	0	100
	%	99.00%	0.50%	0.50%	0.00%	

107-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #

	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	98	0	2	0	100
	Q4	100	0	0	0	100
	%	99.50%	0.00%	0.50%	0.00%	

108-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	94	4	2	0	100
	Q2	94	6	0	0	100
	Q3	97	3	0	0	100
	Q4	97	3	0	0	100
	%	95.50%	4.00%	0.50%	0.00%	

109-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	1	0	0	100
	Q3	98	1	1	0	100
	Q4	100	0	0	0	100
	%	99.25%	0.50%	0.25%	0.00%	

65-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	99	0	1	0	100
	Q3	98	0	2	0	100
	Q4	99	1	0	0	100
	%	98.75%	0.25%	1.00%	0.00%	

66-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	97	1	2	0	100
	Q4	100	0	0	0	100
	%	99.25%	0.25%	0.50%	0.00%	

67-naïve		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	0	1	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	99.75%	0.00%	0.25%	0.00%	

68-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

69-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	98	2	0	0	100

	Q2	99	1	0	0	100
	Q3	100	0	0	0	100
	Q4	99	0	1	0	100
	%	99.00%	0.75%	0.25%	0.00%	

145-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	0	1	0	100
	Q3	98	1	1	0	100
	Q4	99	1	0	0	100
	%	99.00%	0.50%	0.50%	0.00%	

146-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	99	0	1	0	100
	Q4	98	0	2	0	100
	%	99.25%	0.00%	0.75%	0.00%	

147-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

148-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

149-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

Table 49. Lung Lavage Cell Data at 14 days after the Final Exposure

	4 Quadrants/ 100 cells per quadrant counted				
33-control	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	98	2	0	0	100
Q3	99	0	1	0	100
Q4	100	0	0	0	100
%	99.00%	0.67%	0.33%	0.00%	

34-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	1	0	0	100
	Q3	99	0	1	0	100
	Q4	100	0	0	0	100
	%	99.50%	0.25%	0.25%	0.00%	

35-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	100	0	0	0	100
	Q3	98	0	2	0	100
	Q4	100	0	0	0	100
	%	99.25%	0.00%	0.75%	0.00%	

36-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

37-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	99	0	1	0	100
	%	99.50%	0.00%	0.50%	0.00%	

113-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	99	1	0	0	100
	Q4	98	0	2	0	100
	%	99.25%	0.25%	0.50%	0.00%	

114-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	98	2	0	0	100
	Q2	100	0	0	0	100
	Q3	98	0	2	0	100
	Q4	100	0	0	0	100
	%	99.00%	0.50%	0.50%	0.00%	

115-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	1	0	0	100
	Q2	98	1	1	0	100
	Q3	98	2	0	0	100
	Q4	100	0	0	0	100
	%	98.75%	1.00%	0.25%	0.00%	

116-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	0	1	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	99.75%	0.00%	0.25%	0.00%	

117-control		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

41-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	1	0	0	100
	Q3	100	0	0	0	100
	Q4	99	1	0	0	100
	%	99.50%	0.50%	0.00%	0.00%	

42-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	97	2	1	0	100
	%	99.25%	0.50%	0.25%	0.00%	

43-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	1	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	99	1	0	0	100
	%	99.50%	0.50%	0.00%	0.00%	

44-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	97	2	1	0	100
	Q2	99	0	1	0	100
	Q3	98	0	2	0	100
	Q4	100	0	0	0	100
	%	98.50%	0.50%	1.00%	0.00%	

45-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	1	0	0	100
	Q3	98	2	0	0	100
	Q4	100	0	0	0	100
	%	99.25%	0.75%	0.00%	0.00%	

121-low	Macrophages	PMN	Lymphocytes	Eosinophils	total #

	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

122-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

123-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	98	0	2	0	100
	Q3	99	1	0	0	100
	Q4	99	0	1	0	100
	%	98.75%	0.25%	1.00%	0.00%	

124-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	98	1	1	0	100
	Q2	98	1	1	0	100
	Q3	99	1	0	0	100
	Q4	100	0	0	0	100
	%	98.75%	0.75%	0.50%	0.00%	

125-low		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

49-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	99	1	0	0	100
	Q3	98	1	1	0	100
	Q4	100	0	0	0	100
	%	99.00%	0.50%	0.50%	0.00%	

50-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	100	0	0	0	100
	Q3	99	0	1	0	100
	Q4	99	0	1	0	100
	%	99.25%	0.00%	0.75%	0.00%	

51-medium		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100

	Q2	100	0	0	0	100
	Q3	99	0	1	0	100
	Q4	100	0	0	0	100
	%	99.50%	0.00%	0.50%	0.00%	

52-medium	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	99	0	1	0	100
Q3	100	0	0	0	100
Q4	99	1	0	0	100
%	99.50%	0.25%	0.25%	0.00%	

53-medium	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100
Q3	100	0	0	0	100
Q4	100	0	0	0	100
%	100.00%	0.00%	0.00%	0.00%	

129-medium	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	99	1	0	0	100
Q2	99	1	0	0	100
Q3	100	0	0	0	100
Q4	100	0	0	0	100
%	99.50%	0.50%	0.00%	0.00%	

130-medium	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100
Q3	99	0	1	0	100
Q4	100	0	0	0	100
%	99.75%	0.00%	0.25%	0.00%	

131-medium	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100
Q3	100	0	0	0	100
Q4	100	0	0	0	100
%	100.00%	0.00%	0.00%	0.00%	

132-medium	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100
Q3	100	0	0	0	100
Q4	99	0	1	0	100
%	99.75%	0.00%	0.25%	0.00%	

133-medium	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100

	Q3	99	0	1	0	100
	Q4	100	0	0	0	100
	%	99.75%	0.00%	0.25%	0.00%	

57-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	1	0	0	100
	Q3	100	0	0	0	100
	Q4	99	0	1	0	100
	%	99.50%	0.25%	0.25%	0.00%	

58-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	98	2	0	0	100
	Q2	98	1	1	0	100
	Q3	99	1	0	0	100
	Q4	98	1	1	0	100
	%	98.25%	1.25%	3.00%	0.00%	

59-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	99	0	1	0	100
	Q4	100	0	0	0	100
	%	99.75%	0.00%	0.25%	0.00%	

60-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

61-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	0	1	0	100
	Q3	99	0	1	0	100
	Q4	100	0	0	0	100
	%	99.50%	0.00%	0.50%	0.00%	

137-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	99	0	0	1	100
	Q4	99	0	1	0	100
	%	99.50%	0.00%	0.25%	0.25%	

138-high		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	99	0	1	0	100
	Q2	100	0	0	0	100
	Q3	99	0	1	0	100

Q4	100	0	0	0	100
%	99.50%	0.00%	0.50%	0.00%	

139-high	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100
Q3	99	1	0	0	100
Q4	99	1	0	0	100
%	99.50%	0.50%	0.00%	0.00%	

140-high	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100
Q3	100	0	0	0	100
Q4	100	0	0	0	100
%	100.00%	0.00%	0.00%	0.00%	

141-high	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100
Q3	100	0	0	0	100
Q4	100	0	0	0	100
%	100.00%	0.00%	0.00%	0.00%	

73-naive	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	99	0	1	0	100
Q3	100	0	0	0	100
Q4	100	0	0	0	100
%	99.75%	0.00%	0.25%	0.00%	

74-naïve	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	98	0	2	0	100
Q3	100	0	0	0	100
Q4	98	1	1	0	100
%	99.00%	0.25%	0.75%	0.00%	

75-naive	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100
Q3	100	0	0	0	100
Q4	100	0	0	0	100
%	100.00%	0.00%	0.00%	0.00%	

76-naive	Macrophages	PMN	Lymphocytes	Eosinophils	total #
Q1	100	0	0	0	100
Q2	100	0	0	0	100
Q3	99	0	1	0	100
Q4	100	0	0	0	100

	%	99.75%	0.00%	0.25%	0.00%	

77-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	97	2	1	0	100
	Q4	100	0	0	0	100
	%	99.25%	0.50%	0.25%	0.00%	

153-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	97	3	0	0	100
	Q3	99	1	0	0	100
	Q4	100	0	0	0	100
	%	99.00%	1.00%	0.00%	0.00%	

154-naïve		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	1	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	99.75%	0.25%	0.00%	0.00%	

155-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	100	0	0	0	100
	Q3	100	0	0	0	100
	Q4	100	0	0	0	100
	%	100.00%	0.00%	0.00%	0.00%	

156-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	98	2	0	0	100
	Q3	99	1	0	0	100
	Q4	100	0	0	0	100
	%	99.25%	0.75%	0.00%	0.00%	

157-naive		Macrophages	PMN	Lymphocytes	Eosinophils	total #
	Q1	100	0	0	0	100
	Q2	99	0	1	0	100
	Q3	98	0	2	0	100
	Q4	100	0	0	0	100
	%	99.25%	0.00%	0.75%	0.00%	

Lung Lavage Biomarkers

Table 50. Total Protein (µg/ml) in Lung Lavage Fluid 24 hrs after the Final Exposure

Sprague-Dawley Rats									
Controls				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
81	92.593	97.958	90.424	89-Low	103.256	97-Medium	104.697	105-High	104.301
82	86.845	94.946	90.896	90-Low	101.801	98-Medium	104.697	106-High	93.025
83	83.891	84.678	83.090	91-Low	85.338	99-Medium	113.877	107-High	123.846
84	64.261	72.376	62.290	92-Low	104.797	100-Medium	96.707	108-High	109.668
85	91.314	93.212	89.748	93-Low	107.473	101-Medium	114.415	109-High	96.472

F344 Rats									
Rat #/dose	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
Controls				Exposed					
1	116.821	123.022	125.599	9-Low	82.324	17-Medium	110.091	25-High	115.319
2	82.874	88.676	81.382	10-Low	117.432	18-Medium	195.788	26-High	109.919
3	156.346	151.272	149.092	11-Low	124.344	19-Medium	106.179	27-High	155.716
4	65.157	68.945	70.380	12-Low	95.874	20-Medium	79.463	28-High	99.590
5	85.715	83.711	86.473	13-Low	85.337	21-Medium	124.895	29-High	84.570

Table 51. Total Protein (µg/ml) in Lung Lavage Fluid 14 days after the Final Exposure

F344 Rats									
Controls				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
33	68.742	84.080	71.924	41-Low	64.610	49-Medium	92.347	57-High	72.219
34	66.266	71.124	68.275	42-Low	70.806	50-Medium	86.829	58-High	80.549
35	58.398	74.515	65.379	43-Low	59.740	51-Medium	81.724	59-High	70.341
36	62.282	71.038	72.059	44-Low	96.041	52-Medium	75.379	60-High	109.096
37	66.747	74.802	75.469	45-Low	102.982	53-Medium	88.600	61-High	87.426

Sprague-Dawley Rats									
Controls				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
113	130.353	129.131	125.505	121-Low	79.660	129-Medium	130.215	137-High	83.266
114	87.035	98.278	93.477	122-Low	75.134	130-Medium	128.165	138-High	90.377
115	83.972	98.365	89.730	123-Low	71.215	131-Medium	178.888	139-High	76.785
116	91.837	99.181	94.854	124-Low	100.417	132-Medium	118.865	140-High	94.746
117	87.109	100.666	87.709	125-Low	84.488	133-Medium	140.743	141-High	98.741

Table 52. LDH (ng/ml) in Lung Lavage Fluid 24 hrs after the Final Exposure

F344 Rats									
Control				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
1-Control	66.580	73.267	82.553	9-Low	37.324	17-Medium	71.442	25-High	79.416
2-Control	40.083	37.301	46.084	10-Low	76.262	18-Medium	259.132	26-High	86.826
3-Control	167.957	184.315	205.224	11-Low	69.400	19-Medium	55.951	27-High	219.927
4-Control	35.478	35.270	40.210	12-Low	41.453	20-Medium	41.368	28-High	62.269
5-Control	43.259	45.939	52.551	13-Low	48.953	21-Medium	92.808	29-High	46.703

Sprague-Dawley Rats									
Control				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
81-Control	35.209	35.315	44.551	89-Low	35.064	97-Medium	39.158	105-High	49.492
82-Control	37.676	35.969	50.554	90-Low	41.766	98-Medium	37.783	106-High	52.432
83-Control	40.768	38.437	46.958	91-Low	36.764	99-Medium	38.397	107-High	57.246
84-Control	34.110	30.490	39.381	92-Low	42.639	100-Medium	53.585	108-High	52.099
85-Control	42.408	40.732	47.072	93-Low	38.714	101-Medium	39.859	109-High	43.435

Table 53. LDH (ng/ml) in Lung Lavage Fluid 14 days after the Final Exposure

F344 Rats									
Control				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
33-Control	32.177	39.364	35.549	41-Low	50.142	49-Medium	41.491	57-High	38.800
34-Control	33.767	41.679	40.796	42-Low	48.966	50-Medium	65.713	58-High	46.120
35-Control	38.311	33.769	38.753	43-Low	43.426	51-Medium	29.987	59-High	36.712
36-Control	32.825	34.354	34.244	44-Low	80.030	52-Medium	40.622	60-High	73.990
37-Control	39.400	40.854	44.122	45-Low	76.950	53-Medium	28.519	61-High	49.451

Sprague Dawley Rats									
Control				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
113-Control	66.372	79.892	74.585	121-Low	57.288	129-Medium	82.284	137-High	57.246
114-Control	47.539	43.663	46.334	122-Low	78.359	130-Medium	67.568	138-High	43.623
115-Control	55.146	54.213	57.622	123-Low	53.783	131-Medium	129.736	139-High	47.290
116-Control	52.369	50.952	59.077	124-Low	71.204	132-Medium	69.173	140-High	44.693
117-Control	40.765	35.849	43.029	125-Low	60.631	133-Medium	94.430	141-High	56.787

Table 54. N-acetyl-β-D-glucosamidase (mU/ml) in Lung Lavage Fluid 24 hrs after the Final Exposure

F344 Rats									
Control				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
1-Control	1.469	1.772	1.676	9-Low	1.238	17-Medium	1.412	25-High	1.202
2-Control	1.580	1.840	1.572	10-Low	1.340	18-Medium	2.364	26-High	1.136
3-Control	1.291	1.444	No data	11-Low	1.263	19-Medium	1.852	27-High	1.303
4-Control	1.498	1.833	1.662	12-Low	1.145	20-Medium	1.698	28-High	1.252
5-Control	1.418	1.595	1.409	13-Low	1.281	21-Medium	1.699	29-High	1.248

Sprague-Dawley Rats									
Control				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
81-Control	1.621	1.946	1.699	89-Low	0.878	97-Medium	1.452	105-High	1.084
82-Control	1.201	1.507	1.224	90-Low	0.673	98-Medium	1.612	106-High	1.179
83-Control	1.383	1.731	1.329	91-Low	0.684	99-Medium	2.046	107-High	1.020
84-Control	0.906	1.262	1.037	92-Low	0.875	100-Medium	2.254	108-High	1.032
85-Control	1.261	1.564	1.315	93-Low	1.212	101-Medium	1.525	109-High	1.835

Table 55. N-acetyl-β-D-glucosamidase (mU/ml) in Lung Lavage Fluid 14 days after the Final Exposure

F344 Rats									
Control				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
33-Control	1.025	0.867	1.093	41-Low	1.408	49-Medium	1.446	57-High	1.373
34-Control	1.415	1.425	1.548	42-Low	1.655	50-Medium	1.513	58-High	1.645
35-Control	1.180	1.188	1.253	43-Low	1.598	51-Medium	1.069	59-High	1.459
36-Control	1.406	1.266	1.523	44-Low	1.466	52-Medium	1.173	60-High	2.542
37-Control	1.861	1.840	1.957	45-Low	1.668	53-Medium	0.990	61-High	2.104

Sprague-Dawley Rats									
Control				Exposed					
Rat #	Low	Medium	High	Rat #/dose	Low	Rat #/dose	Medium	Rat #/dose	High
113-Control	1.110	0.963	1.098	121-Low	1.048	129-Medium	1.071	137-High	1.484
114-Control	1.026	0.909	1.072	122-Low	1.374	130-Medium	1.321	138-High	1.273
115-Control	0.930	0.873	0.905	123-Low	1.767	131-Medium	1.672	139-High	1.233
116-Control	1.316	1.070	1.541	124-Low	2.070	132-Medium	1.587	140-High	1.244
117-Control	1.387	1.262	1.481	125-Low	1.405	133-Medium	1.878	141-High	1.972

Table 56. β-glucuronidase, MCP-1, and MIP-2 in Lung Lavage Fluid 24 hrs after the Final Exposure

Rat #/dose	β-glucuronidase (nM/ml)	MCP-1 (pg/ml)	MIP-2 (pg/ml)
1-Control	102.486	13.822	30.948
2-Control	132.974	11.988	36.078
3-Control	82.286	6.788	27.118
4-Control	106.324	11.933	29.557
5-Control	112.572	9.482	31.217
9-Low	79.164	10.834	31.442
10-Low	80.560	12.737	29.854
11-Low	103.073	9.961	34.921
12-Low	114.493	32.424	33.311
13-Low	133.825	13.276	33.018
17-Medium	100.152	22.944	41.980
18-Medium	83.377	32.905	44.212
19-Medium	122.156	no data	41.571
20-Medium	120.430	30.895	41.518
21-Medium	94.129	no data	40.422
25-High	98.880	8.584	43.558
26-High	80.384	27.276	40.099
27-High	136.841	26.025	41.522
28-High	112.650	26.785	45.269
29-High	127.106	38.921	41.522
65-Naïve	97.545	8.024	37.636
66-Naïve	104.367	6.698	47.084
67-Naïve	82.876	9.991	50.861
68-Naïve	78.602	23.766	47.628
69-Naïve	93.648	6.347	59.697
81-Control	72.052	18.406	28.258
82-Control	69.505	16.321	25.872
83-Control	73.738	10.204	33.886
84-Control	74.768	16.833	32.181
85-Control	68.680	14.963	34.201
89-Low	68.026	20.747	21.987
90-Low	70.606	25.721	32.837
91-Low	77.945	26.856	16.975
92-Low	74.058	26.199	23.624
93-Low	86.311	48.027	25.374
97-Medium	74.271	no data	32.476
98-Medium	75.293	no data	33.401
99-Medium	86.921	21.795	39.364

Rat #/dose	β-glucuronidase (nM/ml)	MCP-1 (pg/ml)	MIP-2 (pg/ml)
100-Medium	75.644	13.662	44.197
101-Medium	71.943	13.662	32.454
105-High	85.866	39.037	32.946
106-High	82.694	30.555	36.614
107-High	71.495	35.748	40.359
108-High	78.541	49.641	36.988
109-High	76.401	29.469	30.151
145-Naïve	75.812	11.247	47.943
146-Naïve	73.131	7.265	43.216
147-Naïve	68.832	5.831	34.785
148-Naïve	68.372	8.474	41.845
149-Naïve	68.642	12.179	43.314

Table 57. β-glucuronidase, MCP-1, and MIP-2 in Lung Lavage Fluid 14 days after the Final Exposure

Rat #/dose	β-glucuronidase (nM/ml)	MCP-1 (pg/ml)	MIP-2 (pg/ml)
1-Control	102.486	13.822	30.948
2-Control	132.974	11.988	36.078
3-Control	82.286	6.788	27.118
4-Control	106.324	11.933	29.557
5-Control	112.572	9.482	31.217
9-Low	79.164	10.834	31.442
10-Low	80.560	12.737	29.854
11-Low	103.073	9.961	34.921
12-Low	114.493	32.424	33.311
13-Low	133.825	13.276	33.018
17-Medium	100.152	22.944	41.980
18-Medium	83.377	32.905	44.212
19-Medium	122.156	no data	41.571
20-Medium	120.430	30.895	41.518
21-Medium	94.129	no data	40.422
25-High	98.880	8.584	43.558
26-High	80.384	27.276	40.099
27-High	136.841	26.025	41.522
28-High	112.650	26.785	45.269
29-High	127.106	38.921	41.522
65-Naïve	97.545	8.024	37.636
66-Naïve	104.367	6.698	47.084
67-Naïve	82.876	9.991	50.861

Rat #/dose	β-glucuronidase (nM/ml)	MCP-1 (pg/ml)	MIP-2 (pg/ml)
68-Naïve	78.602	23.766	47.628
69-Naïve	93.648	6.347	59.697
81-Control	72.052	18.406	28.258
82-Control	69.505	16.321	25.872
83-Control	73.738	10.204	33.886
84-Control	74.768	16.833	32.181
85-Control	68.680	14.963	34.201
89-Low	68.026	20.747	21.987
90-Low	70.606	25.721	32.837
91-Low	77.945	26.856	16.975
92-Low	74.058	26.199	23.624
93-Low	86.311	48.027	25.374
97-Medium	74.271	no data	32.476
98-Medium	75.293	no data	33.401
99-Medium	86.921	21.795	39.364
100-Medium	75.644	13.662	44.197
101-Medium	71.943	13.662	32.454
105-High	85.866	39.037	32.946
106-High	82.694	30.555	36.614
107-High	71.495	35.748	40.359
108-High	78.541	49.641	36.988
109-High	76.401	29.469	30.151
145-Naïve	75.812	11.247	47.943
146-Naïve	73.131	7.265	43.216
147-Naïve	68.832	5.831	34.785
148-Naïve	68.372	8.474	41.845
149-Naïve	68.642	12.179	43.314

Nasal Lavage Biomarkers

Table 58. Biomarkers Measured in Nasal Lavage Fluid 24 hrs after the Final Exposure

Rat #/dose	total protein (µg/ml)	LDH (ng/ml)	NAG (mU/ml)	β- glucuronidase (nM/ml)	MIP-2 (pg/ml)	MCP-1 (pg/ml)
1-Control	no data	no data	no data	no data	no data	no data
2-Control	30.661	55.140	0.834	64.157	5.630	14.715
3-Control	16.902	29.797	0.525	71.436	3.614	below limit
4-Control	294.806	33.067	4.874	67.631	2.339	below limit
5-Control	50.057	47.174	1.317	66.140	5.359	25.762
9-Low	18.020	40.784	0.611	61.862	no data	no data
10-Low	43.675	45.388	0.896	63.770	no data	no data

Rat #/dose	total protein (µg/ml)	LDH (ng/ml)	NAG (mU/ml)	β- glucuronidase (nM/ml)	MIP-2 (pg/ml)	MCP-1 (pg/ml)
11-Low	16.023	16.405	0.952	321.001	no data	no data
12-Low	123.145	31.436	2.631	72.406	no data	no data
13-Low	103.091	55.346	1.599	72.165	no data	no data
17-Medium	35.063	10.557	0.851	64.985	no data	no data
18-Medium	86.608	29.895	1.802	71.619	no data	no data
19-Medium	91.172	24.488	2.046	199.993	no data	no data
20-Medium	53.805	17.861	1.456	82.668	no data	no data
21-Medium	110.102	47.996	2.557	79.757	no data	no data
25-High	178.471	42.080	3.693	72.186	3.535	16.230
26-High	20.844	22.064	0.800	69.872	3.886	16.294
27-High	24.638	22.305	0.861	66.738	5.809	18.121
28-High	63.774	30.589	1.477	82.668	1.980	30.416
29-High	25.447	24.083	0.880	70.887	2.094	11.095
65-Naïve	143.240	79.319	2.977	73.049	no data	no data
66-Naïve	76.645	134.894	2.373	77.992	no data	no data
67-Naïve	328.141	201.065	4.592	68.624	no data	no data
68-Naïve	102.481	88.228	2.925	76.893	no data	no data
69-Naïve	143.219	178.761	3.466	71.946	no data	no data
81-Control	64.222	40.239	1.949	68.999	5.867	33.901
82-Control	53.601	50.786	1.081	65.851	4.190	below limit
83-Control	28.910	19.518	0.584	64.168	4.217	below limit
84-Control	122.396	33.585	2.650	66.972	7.239	22.83
85-Control	44.408	26.940	1.063	82.519	5.071	below limit
89-Low	21.052	21.945	0.917	79.606	no data	no data
90-Low	37.943	18.974	1.169	94.656	no data	no data
91-Low	37.044	27.947	1.036	82.108	no data	no data
92-Low	30.135	36.024	1.315	79.412	no data	no data
93-Low	97.443	69.925	2.220	67.945	no data	no data
97-Medium	24.752	19.859	0.776	66.482	no data	no data
98-Medium	478.373	91.443	3.993	62.778	no data	no data
99-Medium	37.321	34.327	1.527	76.168	no data	no data
100-Medium	53.412	49.718	2.725	76.377	no data	no data
101-Medium	69.994	28.807	2.220	70.247	no data	no data
105-High	102.579	35.020	3.100	69.078	4.746	28.230
106-High	48.170	45.280	1.803	70.117	5.723	32.334
107-High	54.073	53.411	1.113	65.602	2.950	33.554
108-High	73.960	30.317	1.662	84.330	4.091	12.912
109-High	43.599	41.536	1.812	74.087	6.150	36.949
145-Naïve	52.116	54.049	1.633	93.703	no data	no data
146-Naïve	17.911	32.598	1.174	70.821	no data	no data
147-Naïve	28.565	40.116	1.098	91.737	no data	no data

Rat #/dose	total protein (µg/ml)	LDH (ng/ml)	NAG (mU/ml)	β- glucuronidase (nM/ml)	MIP-2 (pg/ml)	MCP-1 (pg/ml)
148-Naïve	30.921	45.517	2.153	93.145	no data	no data
149-Naïve	no data	no data	no data	no data	no data	no data

Table 59. Biomarkers Measured in Nasal Lavage Fluid 14 days after the Final Exposure

Rat #/dose	Total protein (µg/ml)	LDH (ng/ml)	NAG (mU/ml)	β-glucuronidase (nM/ml)	MIP-2 (pg/ml)	MCP-1 (pg/ml)
33-Control	153.191	69.972	3.121	70.409	2.216	18.050
34-Control	149.092	47.276	2.215	68.270	1.403	13.719
35-Control	24.879	36.457	0.856	78.709	4.365	21.501
36-Control	158.239	55.061	3.250	67.604	1.826	17.577
37-Control	188.610	49.186	3.325	68.137	2.247	8.503
41-Low	227.586	56.770	4.700	67.388	no data	no data
42-Low	82.455	23.565	1.901	75.869	no data	no data
43-Low	212.154	27.765	4.802	73.027	no data	no data
44-Low	56.430	34.487	1.631	70.528	no data	no data
45-Low	64.276	73.062	1.353	84.975	no data	no data
49-Medium	55.971	12.274	1.304	79.281	no data	no data
50-Medium	35.426	17.621	0.913	82.302	no data	no data
51-Medium	53.874	14.844	1.159	75.029	no data	no data
52-Medium	21.896	20.754	0.825	74.718	no data	no data
53-Medium	185.754	28.508	2.359	75.258	no data	no data
57-High	28.635	60.744	1.527	78.442	7.607	24.249
58-High	34.611	51.252	1.998	81.897	5.965	22.938
59-High	24.899	46.578	1.044	87.271	4.404	16.328
60-High	23.335	44.776	0.841	76.113	2.724	11.827
61-High	41.035	74.042	1.678	103.915	5.540	18.465
73-Naïve	173.215	83.127	6.709	82.480	no data	no data
74-Naïve	120.539	187.850	3.757	97.973	no data	no data
75-Naïve	243.112	207.973	2.800	67.491	no data	no data
76-Naïve	215.615	113.691	5.647	73.858	no data	no data
77-Naïve	112.406	148.172	3.154	74.023	no data	no data
113-Control	41.528	29.762	1.486	68.099	4.608	10.543
114-Control	111.209	8.822	2.977	69.892	1.272	11.086
115-Control	68.790	26.742	2.940	83.572	4.491	8.097
116-Control	17.386	24.874	1.243	81.487	3.454	9.742
117-Control	16.830	11.715	0.872	70.962	4.699	9.518
121-Low	28.049	8.711	1.254	64.113	no data	no data
122-Low	31.343	15.882	2.355	84.306	no data	no data
123-Low	25.024	26.128	1.159	69.033	no data	no data

Rat #/dose	Total protein (µg/ml)	LDH (ng/ml)	NAG (mU/ml)	β-glucuronidase (nM/ml)	MIP-2 (pg/ml)	MCP-1 (pg/ml)
124-Low	84.169	40.503	5.553	71.348	no data	no data
125-Low	132.017	76.191	1.554	69.586	no data	no data
129-Medium	41.161	27.337	1.696	88.569	no data	no data
130-Medium	38.795	28.630	1.474	78.552	no data	no data
131-Medium	53.180	39.982	1.605	407.940	no data	no data
132-Medium	31.559	42.150	2.663	83.241	no data	no data
133-Medium	37.414	34.677	1.520	80.519	no data	no data
137-High	29.324	21.082	1.566	183.168	5.822	20.031
138-High	54.816	36.086	1.650	66.149	3.069	26.361
139-High	18.604	18.453	1.252	63.937	5.251	16.269
140-High	61.565	24.605	1.482	93.353	2.703	25.423
141-High	37.037	19.543	1.935	74.424	4.951	18.986
153-Naïve	192.612	50.353	2.851	66.269	no data	no data
154-Naïve	137.245	28.794	2.715	74.307	no data	no data
155-Naïve	34.347	27.206	1.131	91.467	no data	no data
156-Naïve	31.615	12.236	0.965	214.654	no data	no data
157-Naïve	151.594	35.836	1.828	64.233	no data	no data

Spleen Cell Phenotypes

Table 60. Spleen Cell Phenotypes in F344 Rats 24 hrs after the Final Exposure (percent expression of surface markers; * indicates label)

	Assay #1		Assay #2		Assay #3		Assay #4	
	CD45RA (PE)*	CD11b (FITC)*	CD161a (PE)*	CD3 (FITC)*	CD3 (PE)*	CD8b (FITC)*	CD3 (PE)*	CD4 (FITC)*
Naive (1)	50	20	12	39	50	1	41	10
Naive (2)	50	9	16	35	48	1	43	12
Naive (3)	51	9	14	40	51	1	45	10
Naive (4)	49	7	13	36	49	1	47	8
Naive (5)	52	8	14	37	50	1	41	15
Control (1)	60	10	14	44	45	1	40	14
Control (2)	48	9	12	40	51	1	45	10
Control (3)	58	11	13	38	50	1	44	11
Control (4)	50	8	13	40	49	1	43	11
Control (5)	50	8	12	38	49	1	42	9
Low (1)	39	8	13	41	48	1	46	10
Low (2)	55	9	13	39	48	1	40	8
Low (3)	43	8	13	41	46	1	46	10
Low (4)	45	9	13	40	45	1	39	13
Low (5)	53	8	13	39	46	1	39	9
Med (1)	47	9	14	40	43	1	41	12

	Assay #1		Assay #2		Assay #3		Assay #4	
	CD45RA (PE)*	CD11b (FITC)*	CD161a (PE)*	CD3 (FITC)*	CD3 (PE)*	CD8b (FITC)*	CD3 (PE)*	CD4 (FITC)*
Med (2)	42	8	14	39	46	1	42	11
Med (3)	50	8	14	38	46	1	43	11
Med (4)	50	10	14	39	45	1	44	13
Med (5)	47	8	14	38	44	1	41	12
High (1)	46	8	14	39	47	1	41	12
High (2)	46	11	16	37	43	1	42	8
High (3)	44	9	15	38	44	1	37	12
High (4)	44	9	16	34	47	1	43	11

Table 61. Spleen Cell Phenotypes in F344 Rats 14 days after the Final Exposure (percent expression of surface markers; * indicates label)

	Assay #1		Assay #2		Assay #3		Assay #4	
	CD45RA (PE)*	CD11b (FITC)*	CD161a (PE)*	CD3 (FITC)*	CD3 (PE)*	CD8b (FITC)*	CD3 (PE)*	CD4 (FITC)*
Naive (1)	44	7	10	38	53	1	49	6
Naive (2)	50	7	13	37	42	1	49	7
Naive (3)	49	6	11	35	50	1	50	6
Naive (4)	51	7	12	37	49	1	51	7
Naive (5)	47	5	12	38	55	1	57	7
Control (1)	49	8	13	34	51	1	49	8
Control (2)	52	8	13	37	56	1	48	8
Control (3)	55	10	15	32	51	1	50	7
Control (4)	53	8	13	37	52	1	47	8
Control (5)	51	10	14	36	54	1	44	7
Low (1)	51	9	14	38	57	1	53	7
Low (2)	45	8	13	38	55	1	47	8
Low (3)	54	9	14	35	53	1	53	6
Low (4)	48	9	13	38	59	1	52	7
Low (5)	50	9	14	38	56	1	61	6
Med (1)	48	8	13	36	55	1	52	5
Med (2)	47	8	12	37	57	1	50	8
Med (3)	48	7	12	33	54	1	51	8
Med (4)	48	9	13	34	54	1	47	8
Med (5)	54	7	12	39	51	1	50	5
High (1)	51	8	16	34	53	1	48	9
High (2)	51	9	13	37	49	1	47	9
High (3)	53	7	13	35	57	1	52	8
High (4)	49	9	14	36	49	1	48	8
High (5)	48	9	14	34	53	1	51	8

Table 62. Spleen Cell Phenotypes in Sprague-Dawley Rats 24 hrs after the Final Exposure
(percent expression of surface markers; * indicates label)

	Assay #1		Assay #2		Assay #3		Assay #4	
	CD45RA (PE)*	**CD11b (FITC)***	**CD161a (PE)***	**CD3 (FITC)***	**CD3 (PE)***	**CD8b (FITC)***	**CD3 (PE)***	**CD4 (FITC)***
Naive (6)	57	9	6	43	50	1	40	9
Naive (7)	48	6	11	36	51	1	44	8
Naive (8)	54	6	10	32	53	2	45	8
Naive (9)	49	5	9	39	59	1	51	5
Naive (10)	55	6	6	34	39	1	38	7
Control (6)	44	8	11	34	47	1	31	10
Control (7)	54	6	not avail.	not avail.	43	1	39	11
Control (8)	49	6	9	34	44	1	40	10
Control (9)	48	6	5	44	62	1	54	5
Control (10)	44	9	10	40	56	1	51	9
Low (6)	56	6	6	38	47	1	32	7
Low (7)	57	7	6	38	46	1	41	8
Low (8)	46	5	6	44	43	1	41	6
Low (9)	43	7	11	31	46	1	38	9
Low (10)	40	7	5	45	61	1	56	6
Med (6)	61	6	10	31	41	1	38	7
Med (7)	47	7	10	39	51	1	35	12
Med (8)	44	8	9	39	62	1	55	8
Med (9)	45	8	12	36	43	1	45	9
Med (10)	53	6	12	36	50	1	45	7
High (6)	53	7	11	31	43	1	37	2
High (7)	51	6	6	38	46	1	44	7
High (8)	40	7	11	37	51	1	47	6
High (9)	50	7	5	37	43	1	41	5
High (10)	49	8	6	39	47	1	45	11

Table 63. Spleen Cell Phenotypes in Sprague-Dawley Rats 14 days after the Final Exposure
(percent expression of surface markers; * indicates label)

	Assay #1		Assay #2		Assay #3		Assay #4	
	CD45RA (PE)*	**CD11b (FITC)***	**CD161a (PE)***	**CD3 (FITC)***	**CD3 (PE)***	**CD8b (FITC)***	**CD3 (PE)***	**CD4 (FITC)***
Naive (6)	48	7	4	49	66	1	57	5
Naive (7)	55	5	9	42	60	1	45	7
Naive (8)	61	7	10	32	50	1	53	3
Naive (9)	45	5	5	40	54	1	46	5
Naive (10)	50	6	5	36	47	1	57	7
Control (6)	55	8	9	37	51	1	49	5
Control (7)	48	7	8	35	53	1	44	7
Control (8)	56	9	9	36	49	1	50	7
Control (9)	56	7	9	39	53	1	41	7
Control (10)	61	7	9	36	44	1	58	7

	Assay #1		Assay #2		Assay #3		Assay #4	
	CD45RA (PE)*	**CD11b (FITC)***	**CD161a (PE)***	**CD3 (FITC)***	**CD3 (PE)***	**CD8b (FITC)***	**CD3 (PE)***	**CD4 (FITC)***
Low (6)	59	8	9	47	67	1	51	7
Low (7)	60	9	11	36	56	1	50	8
Low (8)	61	8	6	38	50	1	52	6
Low (9)	54	7	9	37	55	1	53	6
Low (10)	50	6	4	45	57	1	58	8
Med (6)	52	5	4	46	57	1	68	4
Med (7)	50	7	4	49	68	1	44	6
Med (8)	60	8	4	37	46	1	53	6
Med (9)	50	8	4	48	55	1	50	6
Med (10)	49	8	8	39	51	1	56	8
High (6)	52	7	13	40	69	1	64	5
High (7)	50	10	5	50	55	1	54	6
High (8)	51	6	8	44	50	1	47	7
High (9)	54	9	12	35	47	1	45	7
High (10)	46	8	10	34	58	3	not available	not available

Pathology Summary Report

Systemic Metabolic Response In Rats (*Rattus norvegicus*)
Exposed To Jet A Biphasic Atmospheres

Protocol Number: 0086
Date: 9 March 2007

Study Director: Gail Chapman, PhD
Study Pathologist: Randall Rietcheck, DVM, DACVP

NARRATIVE PATHOLOGY REPORT for Accession Nos. 060761–060820

History:
Female Sprague-Dawley and Fischer 344 rats were exposed to Jet A vapor/aerosol or air 7 days/week, 1.5 hours/day for 14 days. Urine and blood samples were obtained at various time points before, during, and after exposure. Animals were sacrificed by 70% CO_2 exposure 24 hrs after the last Jet A or air exposure and metabolite profiles in the blood and urine were analyzed. A separate set of animals were also sacrificed by injecting sodium pentobarbital i.p. 24 hours and14 days after the last Jet A exposure for histopathologic examination.

Gross observations:
None presented.

Microscopic findings:
The histopathologic diagnoses are listed on individual animal Pathology Report forms.

Comment:
The histopathologic diagnoses are listed on individual animal report forms and in comment boxes of the attached electronic "0086 Summary Worksheet 060761–060820". Subjective severity scores for each animal are listed as follows with a lower repair score (grade) indicating a less severe finding: 1 = minimal; 2 = mild; 3 = moderate; 4 = marked/severe. A plus (+) mark added to a severity score indicates that the observed lesion would grade somewhere between that score and the next higher severity score, but the lesion is typically not extensive or severe enough to warrant marking it at the higher score. Tissues collected for histopathological evaluation include brain, heart, thymus, lungs, liver, spleen, kidneys, stomach, small and large intestine, ovary, and uterus.

Most lesions diagnosed in various tissues during the evaluation and graded as either minimal or mild are considered incidental findings, which are normally described as background pathology and are discussed further below. These lesions are usually attributed to species characteristics, age, gender, or due to dietary or antigenic influence.

Minimal to mild subacute inflammation (predominantly lymphocytic, with rare plasma cells, eosinophils or neutrophils) within the livers of study animals appears to be of similar incidence to background hepatic infiltrates found in most laboratory rats. The presence of these small foci of inflammatory cells within portal areas and randomly scattered within sinusoids is likely due to incidental bacteria within the enterohepatic system.

Mineralization within renal tubules is present in many study animals. This change is a common finding in certain strains of laboratory rats, often near the corticomedullary junction. It occurs more commonly in female rats and is considered an incidental finding usually associated with the level of hydration. These lesions of minimal to mild severity are considered incidental, background findings. A minimal lesion is interpreted as scattered foci occupying less than 10% of the renal cortex; a mild score tends to be more diffuse occupying 10-25% of the cortex, moderate 26-50% involvement, and a severe grading denotes greater than 50-75% involvement. Additional renal lesions include multifocal areas of proximal tubule epithelial cell alteration (tubular hyperplasia/regeneration), interstitial mononuclear infiltrates (interpreted as lymphocytes), and occasional interstitial or periglomerular fibrosis. These renal changes may represent early manifestations of chronic progressive nephropathy (CPN), a spontaneous disease of certain strains of laboratory rats. Lesions of CPN can appear as early as 3-4 months of age, but it is more common and severe in males. The finding of lymphoplasmacytic pyelitis in one rat (060812, medium dose) is possibly due to an ascending lower urinary tract infection eliciting this antigenic response.

Histiocytic alveolar infiltrates present in the lungs of several rats are judged to be within normal limits and morphology for resident alveolar macrophages. In several rats, infiltrates composed of small numbers of eosinophils or mononuclear cells are present around small caliber arterioles within lung sections. Although the cause is unknown, they are a common, incidental finding.

Histological evidence of edema separating smooth muscle fibers and lymphangiectasia is present within the uterine myometrium of several control and test article-exposed animals. All animals are graded within minimal to mild severity for this finding. Although this tissue change is not a commonly seen or reported finding, it does not appear to be test article related based on the distribution among the study groups.

Remaining lesions not commented on above, but that are reported and commented on individual pathology report forms, are considered tissue handling artifact or incidental findings that are not likely clinically significant. These incidental lesions are judged to be unrelated to any test article effect.

Tissues that were collected but not commented on above are also judged to be essentially within normal limits with no indication of change in their functional characteristics or physical presentation. There was no evidence of infectious, toxic, developmental, or neoplastic change or transformation occurring in any of the tissue sections evaluated.

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LTC, Veterinary Corps, US Army
Chief, AFRL/HEPB/Pathology

LIST OF SYMBOLS, ABBREVIATIONS, AND ACRONYMS

β-glucuronidase	βgluc
% of basophils in total WBC	%BASO
% of eosinophils in total WBC	%EOS
% of large, unstained cells in total WBC	%LUC
% of lymphocytes in total WBC	%LYMPH
% of monocytes in total WBC	%MONO
% of neutrophils in total WBC	%NEUT
Basophil concentration	#BASO
Eosinophil concentration	#EOS
Large, unstained cell concentration	#LUC
Lymphocyte concentration	#LYMPH
Monocyte concentration	#MONO
Neutrophil concentration	#NEUT
Association for Assessment and Accreditation of Laboratory Animal Care	AAALAC
Alkaline phosphatase	ALP
Alanine aminotransferase	ALT
Analysis of variance	ANOVA
Aspartate aminotransferase	AST
Broncoalveolar lavage fluids	BALf
Bovine serum albumin	BSA
Blood urea nitrogen	BUN
Complete blood count	CBC
Chemokine (C-C motif) ligand 2	CCL2
Calculated hemoglobin	CH
Calculated hemoglobin concentration, mean	CHCM
Creatinine	CREA
Chemokine (C-X-C motif) ligand 2	CXCL2
Dulbecco's modified Eagle medium	DMEM
Fischer 344	F344
Gas chromatography	GC
Gastrointestinal	GI
Hematocrit (%)	HCT
Hemoglobin distribution width	HDW
High efficiency particulate air	HEPA
Hemoglobin concentration	HGB
Interleukin	IL
Infrared	IR
Jet Fuel-A	Jet A
Jet propulsion fuel-8	JP-8
Lactate dehydrogenase	LDH
Liters per minute	lpm
Mean corpuscular hemoglobin	MCH
Mean corpuscular hemoglobin concentration	MCHC
Monocyte chemoattractant protein 1	MCP-1
Mean corpuscular volume	MCV

Mid-point of exposure	MID
Macrophage inflammatory protein 2	MIP-2
Mass median aerodynamic diameter	MMAD
Mean platelet volume	MPV
N-acteyl-β-D-glucosaminidase	NAG
Phosphate buffered saline	PBS
Phosphorus	PHOS
Platelet concentration	PLT
Prior to exposure	PRE
Pounds per square inch	psi
Red blood cell concentration	RBC
Red cell distribution width	RDW
Roswell Park Memorial Institute	RPMI
Standard error of the mean	SEM
Total bilirubin	TBIL
Toxic hazard research unit	THRU
Tumor necrosis factor alpha	TNFα
Total protein	TP
Termination of study	TS
White blood cell concentration	WBC

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14. ABSTRACT

Two studies were conducted to assess the potential airway and immune effects following subacute (14-day) exposure of female rats to 500, 1000 or 2000 mg/m^3 of Jet-A for 4 hrs/day. The first study used Sprague-Dawley rats; the second study included both Fischer 344 (F344) and Sprague-Dawley rats. In the first study, exposure to 2000 mg/m^3 jet fuel may have caused significant upper airway inflammation on day 7 post-exposure, as indicated by elevated protein and lactate dehydrogenase in nasal lavage fluid, but any inflammation resolved by day 14 post-exposure. The histological examination showed no evidence of infectious or toxic effect, and the occasional presence inflammation or mineralization was clinically insignificant. In the second study, some lung lavage fluid markers were increased at 24 hrs after the final exposure, indicating possible airway injury/inflammation. However, no test article histological changes were observed in the lungs, nasal cavities, or any other tissue of any of the jet fuel exposed animals. Overall, these studies demonstrated limited evidence of effects of 14 days of exposure to Jet A on the airways, immune system, or any other organ or system of female Sprague-Dawley and F344 rats, with no remarkable differences between strains.

15. SUBJECT TERMS
Jet fuel, Jet A, rats, immunotoxicity, lung injury, bronchoalveolar lavage, nasal lavage, inhalation, two-week, vapor and aerosol

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